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The Hand of Time

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SILENT AND MASQUERADING INTRATHORACIC LESIONS*

The Importance of Proper Identification of Lesions Discovered during X-Ray Surveys

RICHARD H. OVERHOLT, M.D.,† AND NORMAN J. WILSON, M.D.

BOSTON

MILLIONS of persons have recently had their chests x-rayed in the mass surveys of large segments of the population now under way. The program at induction centers and in the armed forces, industrial plants and schools is well known. In addition, some form of radiologic screening of the chest is becoming a routine procedure in many clinics and hospitals and in the private practice of many physicians. Thousands of pathologic lesions have been discovered in apparently healthy persons, a large percentage being in the minimal stage, when treatment offers the best chance of cure.

Of this group, the patient who presents one of the most difficult and important problems is the one with a lesion of the chest demonstrated by x-ray and associated with either no symptoms or those so mild that its seriousness and potentialities are unsuspected. These cases present a grave problem to the medical profession. Surveys find, but do not necessarily identify, disease. The proper identification and successful treatment of these early forms of intrathoracic disease demand serious attention.

There is evidence that the danger and the immediate threat of such lesions are too little appreciated. Waiting for time to tell the story is still prevalent. All too often the physician reassures his patient and asks him to return in a few months for a checkup, only to find at that time that a minimal tuberculous focus has developed into moderately advanced or far-advanced disease, or that a small tumor has either metastasized or extended so that it is no longer operable. Roentgenologists likewise frequently advise checkups in a few months in the face of disease processes that carry an immediate and dangerous threat. In the light of present diagnostic and therapeutic possibilities, time becomes a deadly enemy for many patients with intrathoracic lesions.

Recently Goorwitch[1] analyzed the effects of mass surveys in Los Angeles County, California, on the extent of pulmonary involvement in tuberculous males admitted to the Olive View Sanatorium. Although approximately two thirds of the lesions so found were minimal, no reduction occurred in the incidence of far-advanced disease among those entering the sanatorium. Goorwitch explained this by the fact that only a small percentage of those with minimal involvement were admitted. Such statistics leave unanswered the question of what has happened to the thousands of patients with minimal lesions uncovered in surveys and in private practice. To be sure, some of these are lost in the shuffle. Others refuse to enter a sanatorium for treatment. The histories of such cases, however, all too frequently point to the failure of physicians to appreciate the seriousness of the early lesion as the direct cause of the patient's delay in entering the sanatorium for proper treatment.

The same state of affairs exists with carcinoma of the lung. In 1942, Overholt[2] reviewed 153 such cases. Sixty per cent of these patients were not only incorrectly diagnosed by the first physician consulted but were treated on the basis of that diagnosis for long periods of time, an average of twelve months intervening between the onset of symptoms and the establishment of the proper diagnosis. In the average case the physician did not request an x-ray examination for three months after onset, and the correct diagnosis was not made for six months after the pulmonary lesion had been demonstrated by x-ray.

The foregoing facts establish the need for fundamental concepts concerning the diagnosis, evaluation and therapy of intrathoracic lesions. Naturally, the entire subject cannot be covered in a single paper of this kind, and only three outstanding types of condition uncovered in mass surveys will be considered — tuberculosis, carcinoma of the lung and mediastinal tumors.

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Tuberculosis

The evaluation of tuberculous lesions of small or moderate extent that are either asymptomatic or produce extremely mild symptoms presents a serious and difficult problem. These lesions may form early exudative, caseous foci and thus carry an immediate threat or may be predominantly fibrotic and calcific, in which event the danger is more remote. They may be stationary, retrogressive or progressive. The basic problem is that of proving the inactivity or activity of the demonstrated x-ray lesion. It becomes the duty of the

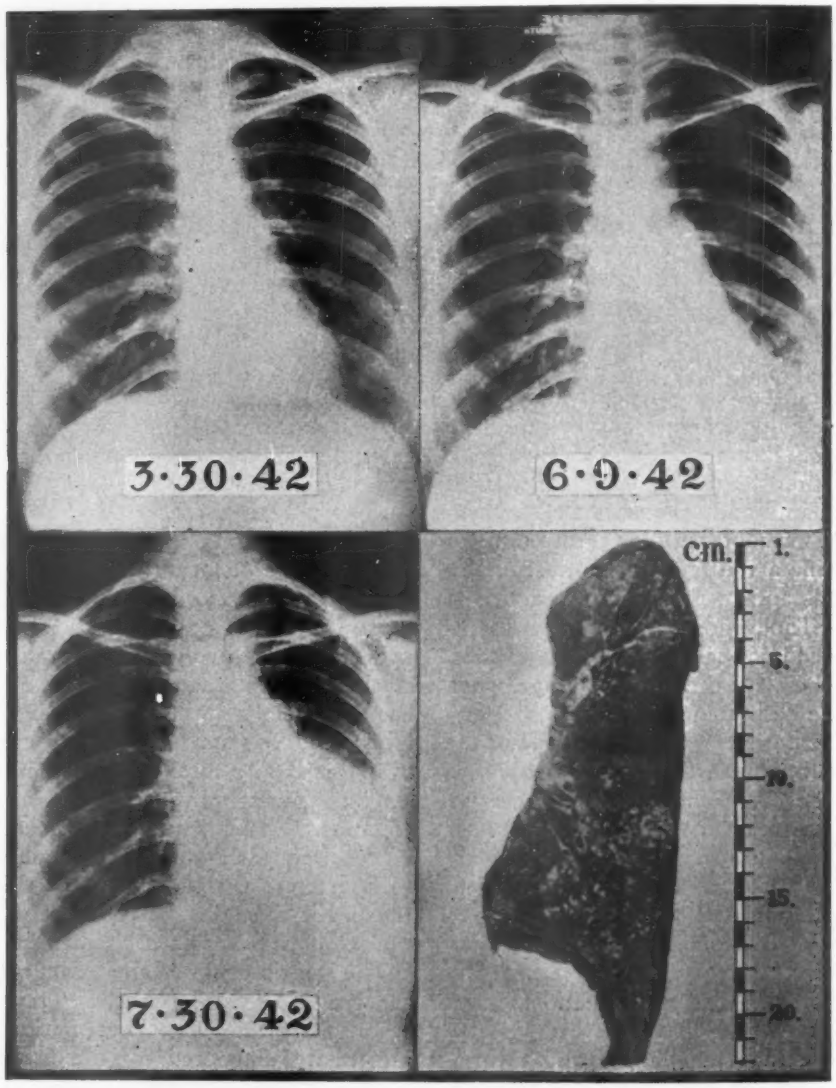

Figure 1. *Case 2094.*

A 29-year-old, married woman, was first seen in March, 1942, complaining of fatigue, low-grade fever and wheezing in the left side of the chest of 3 months' duration. She had been treated for bronchitis with sulfadiazine. A roentgenogram of the chest taken at that time (upper left) revealed a small area of infiltration in the left 2nd interspace. A sputum examination was not performed, and the patient was advised to return in 3 months for another x-ray examination of the chest. A chest x-ray film taken June 9 (upper right) showed little, if any, significant changes, and the patient's symptoms and general condition had not changed since the time of her first examination three months earlier. In a film taken July 30 (lower left), just six weeks later, there was a mediastinal shift, and increased density at the left base was interpreted as atelectasis; the infiltration in the left upper lobe had also increased. The patient's symptoms had increased, and bronchoscopy revealed a marked tuberculous ulcer stenosis of the left main bronchus; the sputum was positive. A left pneumonectomy was performed, and the patient is living and well today, with a persistently negative sputum. In the surgical specimen (lower right) the entire left lower lobe was literally riddled with caseous nodules and numerous areas of caseation were also present in the upper lobe; there was no cavity. Comment: *This case illustrates pulmonary tuberculosis masquerading as "asthmatic bronchitis." It also demonstrates rapid progression of disease within the space of a few weeks, which was the direct result of the bronchial lesion in this particular case. A sputum examination early in the course of the patient's illness would have established the diagnosis and would have brought her under proper treatment. This possibly might have averted the marked spread of the tuberculosis.*

physician not only at once to guard patients with innocuous lesions against long periods of unnecessary therapy, but — what is more important — to protect those with active lesions by giving prompt and energetic treatment.

Evaluation of the Patient

The evaluation of the patient who harbors the tuberculous focus is of prime importance. The age, sex, race and socioeconomic status are the chief factors to be considered.[3]

Age. The evidence gained in mass surveys and in the study of serial x-ray films demonstrates that early tuberculous infiltration usually occurs between adolescence and the age of thirty. These lesions represent a focus of tuberculous bronchopneumonia, with a predominant tendency toward central caseation, excavation and bronchial spread. They constitute an immediate threat, and therapy must therefore be prompt and adequate. In the later decades of life, more of the chronic productive fibroid forms of tuberculosis are seen. Some of these patients require therapy because of residual or renewed activity. In others, the lesion has been stable for many years and requires no therapy. In the latter type of case, a period of watchful waiting is justifiable provided that complete studies have failed to show any signs of activity.

Sex. It is also during the second and third decades that the factor of sex exerts its strongest influence. Tuberculosis in young women tends to be more active and fatal than in men of the same age group.

Race. Although the influence of race is strongly disputed, there can be little doubt that under existing circumstances in most communities Negroes exhibit a lower resistance to tuberculosis than do Whites. This is evidenced by their greater tendency to develop acute pneumonic lesions and by their predisposition to dissemination of the infection through the lymphatics and blood stream.

Socioeconomic factors. The patient's occupation and station in life also influence the prognosis. Clinical and epidemiologic studies show that poverty and debilitating working conditions are likely to be associated with progressive tuberculosis.

These factors are vital not only in evaluating the lesion but in prescribing treatment, because they render both steps possible on the basis of the underlying lesion. The clinical data must be interpreted pathologically if judgment is to be accurate and treatment adequate.

Study of the Sputum

When a positive sputum has been found in a patient with a pulmonary infiltration, not only has the diagnosis been confirmed but the need for active therapy has been established. Any lesion shedding tubercle bacilli harbors some activity. Nevertheless, it must be emphasized that a positive sputum is not a prerequisite for a diagnosis of pulmonary tuberculosis and that a negative sputum does not necessarily rule out activity. A positive sputum may never be demonstrated in inactive lesions and in many active ones of minimal extent. It has been repeatedly shown, however, that a sufficiently rigid study of the sputum will show it to be positive in the vast majority of active tuberculous lesions.

Two factors influence the accuracy of sputum examinations — the length of time over which the specimens have been collected and the method by which they have been examined. The examination of single specimens by the routine smear method is notoriously unreliable. In fact, it is so inefficient that its use as a diagnostic procedure should be condemned. The use of a concentration technic increases positive findings by about 30 per cent. Pooled specimens, the sputum having been collected from two to seven days, further increase positive results. Multiple cultures and guinea-pig inoculations of pooled specimens should always be employed before one concludes that the sputum is negative. In the event that sputum cannot be produced, a study of gastric washings usually reveals the presence of tubercle bacilli if the pulmonary process is active. Secretions from the lungs that are carried to the upper air passages by ciliary motion of the mucosa and by gravity are swallowed during sleep, so that the gastric specimen should be taken in the morning and before breakfast. Acid-fast organisms that are not tubercle bacilli are frequently found in the gastric specimen. For this reason, they should be identified by culture and guinea-pig inoculation.

Pinner and Werner[4] state that over 99 per cent of patients with active tuberculosis are found to have tubercle bacilli in secretions from the lungs if all methods of examination are utilized. Thus, when these tests are repeatedly negative in a patient with a progressive pulmonary infiltration, the lesion is probably nontuberculous and other diagnostic procedures are indicated. For example, we have proved the presence of primary cancer in a considerable number of sputum-negative patients who had been treated for months for tuberculosis by bed rest and even pneumothorax.

Leukocytic Index and Erythrocyte Sedimentation Rate

An altered leukocytic index or an elevated erythrocyte sedimentation rate usually indicates activity of the tuberculous lesion. Here again, however, it must be emphasized that an active, progressive tuberculous focus may produce too little systemic reaction to cause any abnormality in either of these findings. In fact, the vast majority

of early lesions are associated with no change in the leukocytic index and no elevation of the sedimentation rate, so that these laboratory tests are of value only when they show abnormality.

Evaluation of the Roentgenogram

It is evident that the clinical evaluation of the patient and the study of the sputum, leukocytic index and erythrocyte sedimentation rate establish the activity of the pulmonary lesion in some cases. An extremely important group remains in which the only significant evidence of trouble is the lesion demonstrated on the x-ray film. Once a single survey film has located an abnormal shadow, it is necessary to follow up this examination with a more comprehensive x-ray study. Fluoroscopy, stereoscopic exposures, spot films and oblique exposures often yield additional information. The precise location in respect to pulmonary segments should be determined, and the size and character of the abnormal shadow in all its dimensions should be known at the beginning. At times the character of the x-ray shadow strongly indicates the presence of activity. Most dense and homogeneous lesions with ill-defined, fuzzy edges are exudative. More frequently, the activity of the process is indicated by serial roentgenograms. Any change, whether it be progression or resolution, indicates an active lesion. It is essential to realize that such foci resolve to a point at which little or no change is discernible from month to month, and yet remain a constant threat because of residual foci of caseation. After the x-ray fails to reveal any change in the lesion, it requires months, and frequently years, for the processes of healing and fibrous encapsulation to become sufficiently firm to offer adequate protection against reactivation.

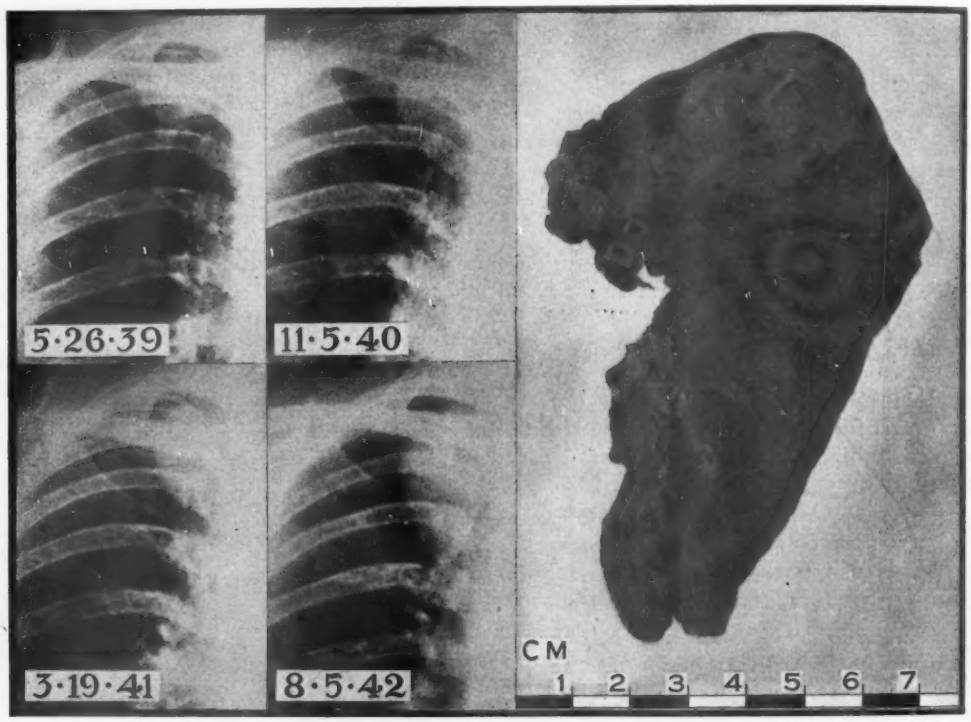

FIGURE 2. *Case 2194.*

This 41-year-old single woman was first seen in October, 1942. A mass in the right upper lobe (upper left) had been discovered elsewhere in May, 1939 and had been followed by periodic chest x-ray films. The patient had always been asymptomatic. Repeated sputum examinations were negative, as was bronchoscopy. Bronchography revealed no distortion of the bronchi in the right upper lobe. The serial x-ray films (lower left) had shown a gradual increase in size of the mass, and an exploratory thoracotomy was advised. At operation on November 12, a large mass was found in the right upper lobe. No lymph nodes were palpable, but a few nodules were felt in the surrounding lung tissue. A diagnosis of tuberculoma was made, and a right upper lobectomy was performed. The patient had an uneventful postoperative course, and she is now asymptomatic, well and working. The surgical specimen (right) showed a large tuberculoma, and pathological examination revealed this mass to be incompletely encapsulated. Two areas of softening in the caseous mass were found, and numerous small tuberculous foci were seen in the surrounding parenchyma. The bronchial lymph nodes showed tuberculous involvement. Comment: *This tumor in the right upper lobe was discovered by routine x-ray examination, but the diagnosis remained uncertain until proved at the time of exploratory thoracotomy.*

It cannot be too strongly emphasized that a minimal tuberculous lesion causing no symptoms, no abnormal physical findings and no alteration of the leukocytic index or erythrocyte sedimentation rate can be, and frequently is, an early focus of disease with serious potentialities and represents an immediate threat.

Treatment

Needless to state, any patient with a positive sputum or clinical evidence of activity requires immediate treatment. It is not the purpose of this discussion to consider in detail the various types of therapy; rather, because of the larger number of minimal lesions in the cases under discussion, it seems timely to restate the fundamental concepts of the treatment of the minimal, and more particularly the early, tuberculous lesion. The following concepts are not original but have been proved over and over again by many studies of the pathogenesis, pathology, resolution and clinical aspects of early tuberculous infiltrations.

The most opportune time to treat tuberculosis is during the phase of the early lesion, when resolution and complete healing are more nearly possible and more easily accomplished than in any later phase of the disease process. The early infiltration tends to caseate and spread, and this is what happens in the majority of untreated cases. On the other hand, most cases treated by strict bed rest undergo resolution and healing.[5]

Progression of such an early minimal lesion may be extremely rapid, with moderately advanced or far-advanced disease resulting in as short a time as a few weeks.[6] The younger the patient, the greater is the possibility of rapid progression. Thus, any lesion in a teen-age person or a young adult should be considered active until proved otherwise by a long period of observation, during which frequent x-ray films should be taken at intervals not exceeding every two weeks. In any case, regardless of age, a policy of watching the lesion with the patient carrying on his normal activities is justifiable only when the lesion is fibrotic and inactive beyond any doubt. To wait for a minimal lesion to spread to prove its activity is to court disaster, for such a procedure not only lengthens and complicates the course of treatment but jeopardizes the patient's chances of recovery.

All patients with early tuberculous lesions should be treated promptly and energetically with strict bed rest, preferably in a sanatorium. The younger the patient, the more rigid and prolonged the treatment should be. The vast majority of early lesions resolve and heal with this treatment. If progression occurs, other measures, such as pneumothorax, may be indicated. It seems important to reemphasize the need for x-ray films taken at intervals of one or two weeks during the first several months because such lesions may spread rapidly. Treatment should be continued for many months after all clinical, laboratory and x-ray evidence of activity have disappeared. This rule is based on the fact that the resolution and fibrous encapsulation of a tuberculous focus are slow processes and continue for at least a few years, during which time any factor that upsets the patient's general resistance is likely to cause an exacerbation.

In 1937, Amberson[5] reported his experiences with x-ray surveys and the treatment of pulmonary tuberculosis in student nurses at Bellevue Hospital, New York City, over a six-and-a-half year period. In this paper he told a story to which all physicians should listen attentively. They need look no further for the proper treatment of the early tuberculous lesion. Amberson states:

> All tuberculosis appearing in student nurses has been discovered early, usually in the form of the early infiltration. Progression or relapse of the lesion in spite of rest treatment has occurred in less than 5 per cent of the cases. All who have completed treatment were able to work, and there have been no deaths from tuberculosis.

This study emphasizes the fundamentals of successful treatment of the early tuberculous focus — early discovery of the lesion and prompt, energetic and prolonged treatment, with bed rest and the judicious supplementary use of collapse measures.

Carcinoma of the Lung

Carcinoma of the lung is a problem that should be of concern to every physician. Statistics show that it represents over 10 per cent of all cases of carcinomas coming to autopsy. In Koletsky's study[7] of 7685 autopsies, the lung was the second most frequent site of primary cancer, being exceeded only by the stomach. Jaffé[8] in a study of 6800 autopsies found it in the third place, with the stomach in the first place and the intestine in the second. All evidence points to an absolute as well as a relative increase in incidence. At least 15,000 people in the United States die each year from cancer of the lung.[2]

Clinical Factors

Carcinoma of the lung, like cancer elsewhere in the body, is a disease of later life, occurring most frequently in persons over forty years of age. It is, however, by no means rare in the fourth decade, and it is occasionally seen in younger patients. It is predominantly a disease of the male sex, being at least four times as frequent in men as in women.

Primary carcinoma of the lung is bronchiogenic in origin. Thus, the signs and symptoms are the results of three processes — local irritation and destructive processes in the bronchus itself, varying degrees of bronchial occlusion and secondary changes in the lung parenchyma. In the very early stages, when the degree of bronchial occlusion is small, the x-ray examination is likely to be negative, as is the physical examination. Although symptoms may be absent at such a time, experience has shown that they tend to occur quite early in the disease. Those oftenest seen at this stage are an irritative, nonproductive, persistent cough and hemoptysis, but localized wheezing is not infrequent. At times, a metastasis from a small tumor is the cause of the first symptoms noted. As the tumor enlarges and the degree of bronchial occlusion becomes greater, the x-ray and physical findings fre-

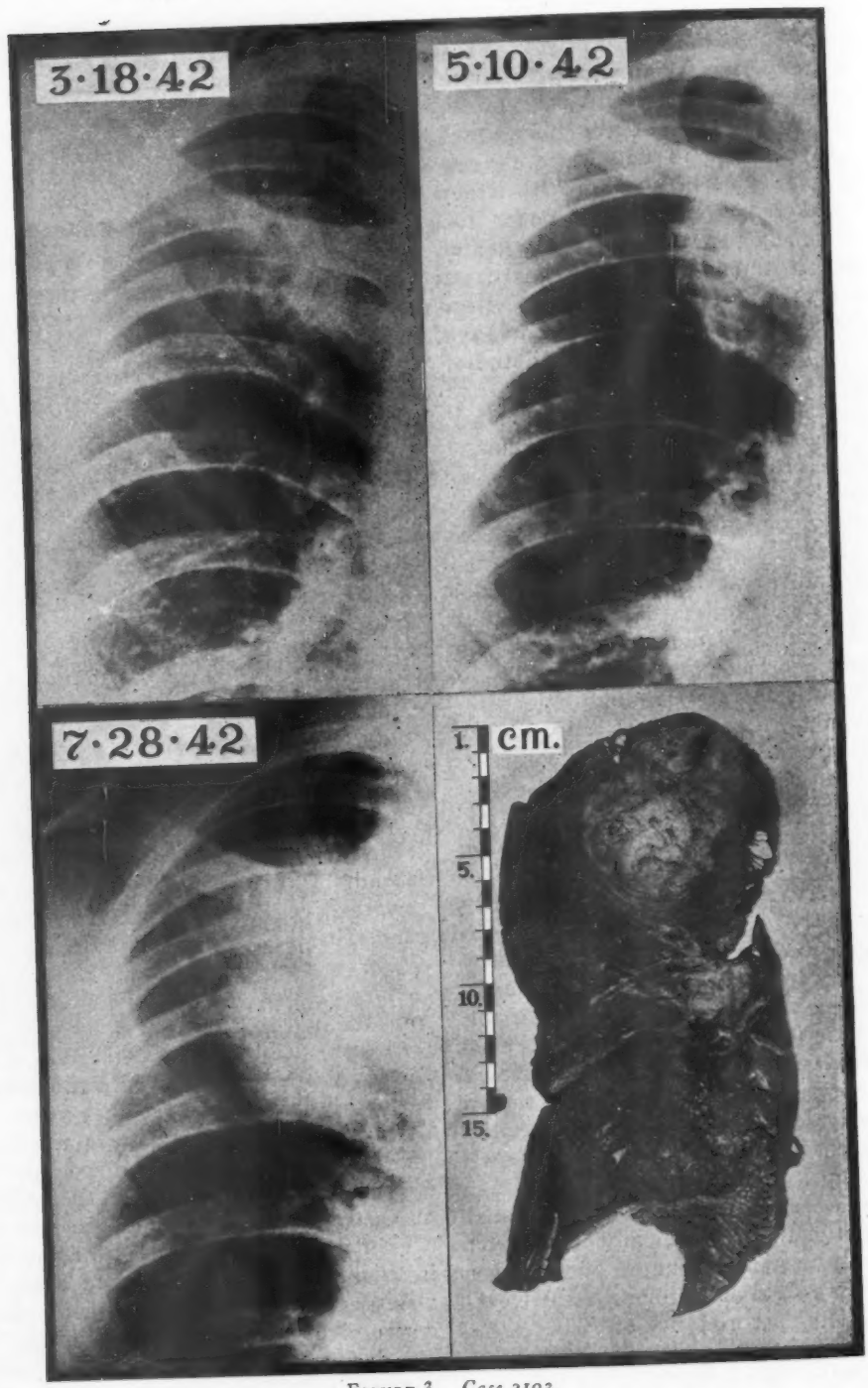

FIGURE 3. *Case 2103.*

This 44-year-old man had complained of slight cough for several years, which was attributed to excessive smoking. In March, 1942, the sputum became blood-streaked. On the basis of the roentgenogram taken on March 18 (upper left), a diagnosis of pulmonary tuberculosis was made in spite of a persistently negative sputum. A roentgenogram taken two months later (upper right) showed progression of disease. The sputum was still negative, but the patient was still being treated for pulmonary tuberculosis. On the basis of a roentgenogram taken on July 28 (lower left), four months after the initial roentgenogram, a diagnosis of tumor was made, and the following month the patient was referred for surgical treatment. Bronchoscopy was negative. Exploratory thoracotomy revealed a large tumor in the right upper lobe, with metastases to the bronchial lymph nodes. No mediastinal nodes were palpable. A palliative right pneumonectomy was performed. The patient made an uneventful recovery and remained well until December, when he developed evidences of metastatic disease, with death in February, 1943. The surgical specimen (lower right) was a Grade III epidermoid tumor, with metastasis to the bronchial lymph node. At the time of autopsy, metastases were found in the spleen, the left adrenal gland and the peritracheal and supraclavicular lymph nodes. Comment: *This case demonstrates bronchiogenic carcinoma masquerading as pulmonary tuberculosis in its early stages. The persistently negative sputum, with a changing x-ray lesion, should have aroused suspicion and indicated further diagnostic procedures. An exploratory thoracotomy at the time of the first roentgenogram would have settled the diagnosis, and pneumonectomy would have offered a better chance of cure. Attention is called to the fact that bronchoscopy was negative even at the time of operation, when metastases had already occurred. This emphasizes the limitations of bronchoscopy in the early diagnosis of bronchiogenic carcinoma and the necessity for exploratory thoracotomy.*

quently indicate an obstructive emphysema of lobular, lobar or multilobar extent. More complete bronchial occlusion leads to atelectasis of similar segments of the lung. If this persists, superimposed infection of the involved parenchyma is the rule.

The x-ray manifestations depend on four factors — the type and location of the tumor, the degree of bronchial occlusion, whether infection of the parenchyma has occurred and whether mediastinal or chest wall extension has taken place. In the early stages, the most frequent x-ray findings are obstructive emphysema or atelectasis of lobular, lobar or multilobar extent. Less often, the tumor itself is seen — notably when it has originated in the periphery of the bronchial tree. Evidence of infection may be superimposed early. Extension to the mediastinum and chest wall, although certainly not a part of the early pathologic life of the tumor, sometimes occurs early in the clinical course.

From this incomplete consideration of bronchiogenic tumors, it can be seen that most of the symptoms usually listed as those produced by carcinoma of the lung, such as pain, excessive sputum, weight loss and cachexia, are as a rule not a part of the early picture. They are the result of extension of the tumor, secondary changes of lung parenchyma and the systemic reaction to both these processes. More frequently, the x-ray film shows definite changes, yet the symptoms are so mild as to cause little suspicion of such a serious underlying lesion. The latter type of case is the one oftenest seen in the early stages in survey work and clinical practice, and is the one on which we wish to focus attention. Most patients are men past middle age with a demonstrated x-ray lesion, accompanied by no symptoms or by mild ones. In many cases the only symptom is a mild cough, which is attributed to cigarette smoking. The clinical picture may mimic that of any of the ordinary diseases of the lungs. The x-ray manifestations may be indistinguishable from those of tuberculosis, bronchiectasis, unresolved pneumonia or suppurative disease. Such patients present a serious problem and one that demands immediate solution. If the lesion is caused by carcinoma, speed in diagnosis and surgical extirpation offer the only chance for cure. In no other disease process is time so dangerous an enemy. Early diagnosis and radical treatment in the early stage frequently lead to successful therapy. Without exception a policy of watchful waiting leads to ultimate death.

Thus, any patient, especially one past middle age, with persistent pulmonary symptoms or an unexplained x-ray lesion* should be immediately subjected to a series of diagnostic tests to prove or disprove the existence of cancer. Whenever possible, tissue should be secured for pathological study, since this is the only sure way to establish the diagnosis.

*All survey or single films that reveal abnormal shadows should be followed by a complete x-ray study of the chest. Fluoroscopy and multiple views that scan the lesion from various angles should be used. Lateral and oblique views are valuable for lobular localization. Often heavy-exposure (Bucky) films are necessary.

Diagnostic Procedures

Search for peripheral metastasis. Careful examination of the cervical lymph nodes and the skin for evidence of metastasis should be made, and suspicious nodes or skin nodules should be removed for pathological study. If the biopsy is positive, the diagnosis is proved and further studies are unnecessary. If there is no evidence of peripheral metastases, bronchoscopy should be the next procedure.

Bronchoscopy. Now that a greater number of cases of early bronchiogenic cancer are being discovered by chest roentgenograms, a revision of the present concept of the value of bronchoscopy as a diagnostic procedure is in order. The medical literature abounds with statistics indicating that 70 to 75 per cent of all bronchiogenic carcinomas originate in the major bronchi and are thus visible through the bronchoscope and accessible for biopsy.

These statistics are misleading in that they apply to all types of tumor without regard to time relations. They are false when applied to early carcinoma of the bronchus. As Gebauer[9] has shown, bronchoscopy if performed early yields negative results in 40 per cent of the cases because the site of origin is beyond bronchoscopic view. In addition to the time relation, the percentage of positive biopsies varies with the type of tumor. For instance, Gebauer demonstrated that 49 per cent of squamous-cell carcinomas originate in the upper lobes or small branch bronchi and that they are not likely to be accessible for biopsy until rather late in the disease. When one considers that epidermoid carcinoma is not only the most frequent but the most curable of all types of lung cancer, the significance of this finding can be realized.

Thus, the actual value of bronchoscopy in the early diagnosis of carcinoma of the lung can be stated in simple terms as follows. It still is the most valuable diagnostic procedure for securing tissue for biopsy. It is, however, an unreliable guide when the results are negative, since it does not in any way exclude the presence of a tumor immediately beyond the vision of the bronchoscopist. A negative bronchoscopy in a patient suspected of having pulmonary cancer thus means only that further diagnostic procedures are indicated. It cannot be emphasized too strongly, since it is a fact not generally recognized, that in the diagnosis of early cancer bronchoscopy is about 50 per cent inefficient.

Bronchography. If there is no evidence of peripheral metastasis and the bronchoscopy results are negative, the next step in the diagnostic procedure may be bronchography. At times, the instillation of lipiodol into the bronchial tree demonstrates

a block in its secondary or finer divisions. Here again, it is important to realize that a negative bronchogram in no way rules out tumor. We bronchoscopy is needed to obtain a biopsy specimen.

Study of sputum for malignant tissue. In the experience of most workers, and especially those in

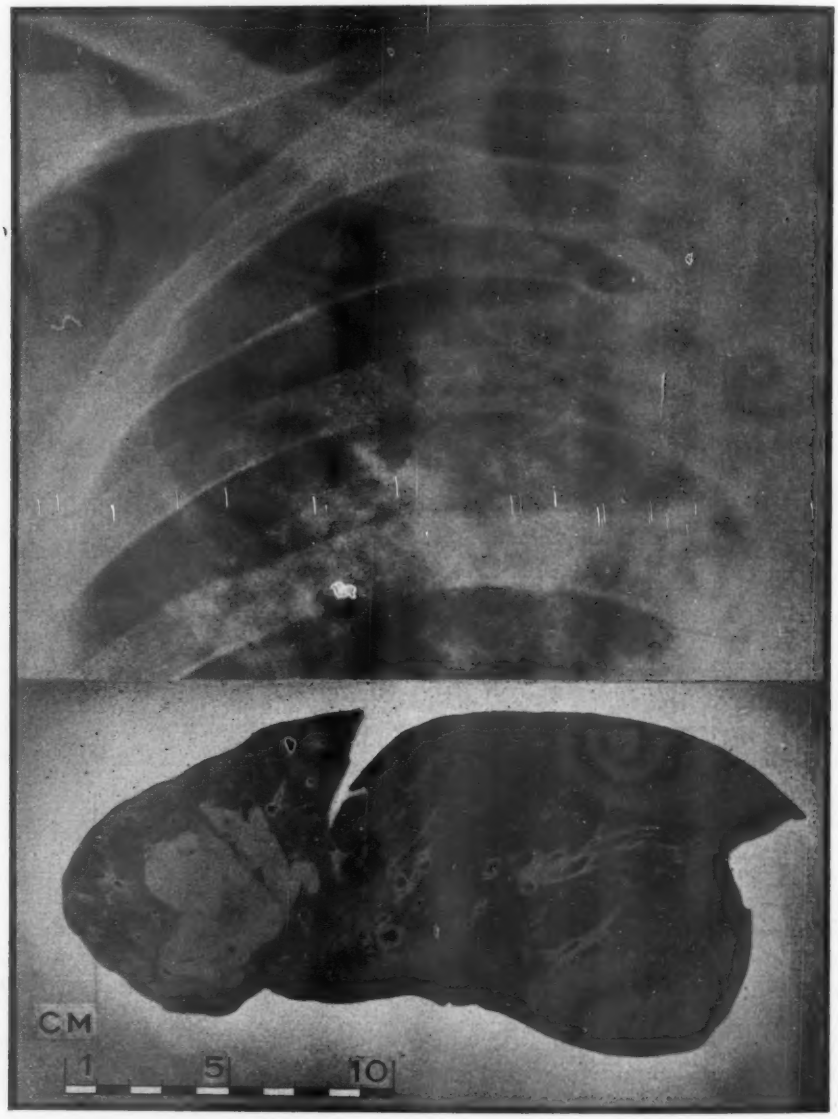

FIGURE 4. *Case 1268.*

This 55-year-old man was first seen on November 24, 1940, at which time he had been under treatment for pulmonary tuberculosis for six months. His history revealed that six months previously he had had a "pneumonia" followed by a chronic cough and expectoration. In spite of a persistently negative sputum, a diagnosis of pulmonary tuberculosis was made, and the patient sent to a sanatorium, where he remained under treatment for six months. While there, his sputum was also negative on all tests. When first seen in November, his weight had dropped from 115 to 95 pounds. He complained of cough, expectoration of blood-streaked sputum, night sweats and a dull pain in the right shoulder. Bronchoscopy revealed a mass protruding from the orifice of the right upper lobe, but biopsy of this revealed only necrotic tissue. Exploratory thoracotomy was performed. A large tumor was found in the right upper lobe. One mediastinal lymph node was enlarged, and frozen section of this revealed epidermoid carcinoma. A palliative pneumonectomy was performed. The patient did well for a few months and then rapidly became worse, dying in November, 1941. The roentgenogram taken just before operation (upper) suggests pulmonary tuberculosis, there being no indication of the large tumor mass found in the surgical specimen (lower). Comment: *The chest roentgenogram in this case suggested pulmonary tuberculosis. The clinical course and the persistently negative sputum, however, should have indicated bronchoscopy and exploratory thoracotomy six months before the patient was referred for these procedures. It is possible that a curative type of pulmonary resection might have been performed at that time.*

believe that bronchography shou'd never be performed unless the results of bronchoscopy are negative because even if it demonstrates the tumor, the average laboratory, the demonstration of cancerous tissue in the sputum has proved to be extremely disappointing. It is not recommended

as a routine diagnostic procedure in cases suspected of being cancer. If it is used, it is of significance only when positive.

Aspiration biopsy. Aspiration biopsy is not without danger and should be used only in cases that are obviously inoperable, especially when the tumor is located peripherally. In cases considered operable, it seems to be unnecessary. A positive aspiration biopsy calls for surgical exploration to determine resectability. A negative one does not rule out tumor, and therefore surgical exploration must be done to settle both the diagnosis and the question of operability.

Exploratory thoracotomy. Exploratory thoracotomy in suspected cases of tumor is a procedure that is used too little and too late. With the present-day status of thoracic surgery, this operation is on a par with abdominal exploration regarding safety and accuracy. In spite of this, there is still a great deal of hesitancy on the part of the average physician to refer a patient with unexplained pulmonary disease for exploratory thoracotomy. For many years, abdominal exploration has been an accepted procedure in establishing the diagnosis of unexplained tumor masses and lesions in the abdominal cavity. It is essential that physicians develop a similar attitude toward exploratory thoracotomy, if it is ever to be possible to treat a large proportion of cases of pulmonary cancer in the early stages. The value of this procedure can be gleaned from the fact that in 24 per cent of 153 cases reported by Overholt[10] in 1942, the diagnosis was established and treatment was carried out on the basis of a biopsy specimen secured at exploratory thoracotomy. The sooner the pathologic process is discovered, the more valuable as a diagnostic procedure exploratory thoracotomy becomes. We believe that it should be carried out immediately to establish the diagnosis in all patients suspected of having pulmonary cancer, even though the bronchoscopy is negative, except, of course, for those with proved metastasis. This concept is based on three es-

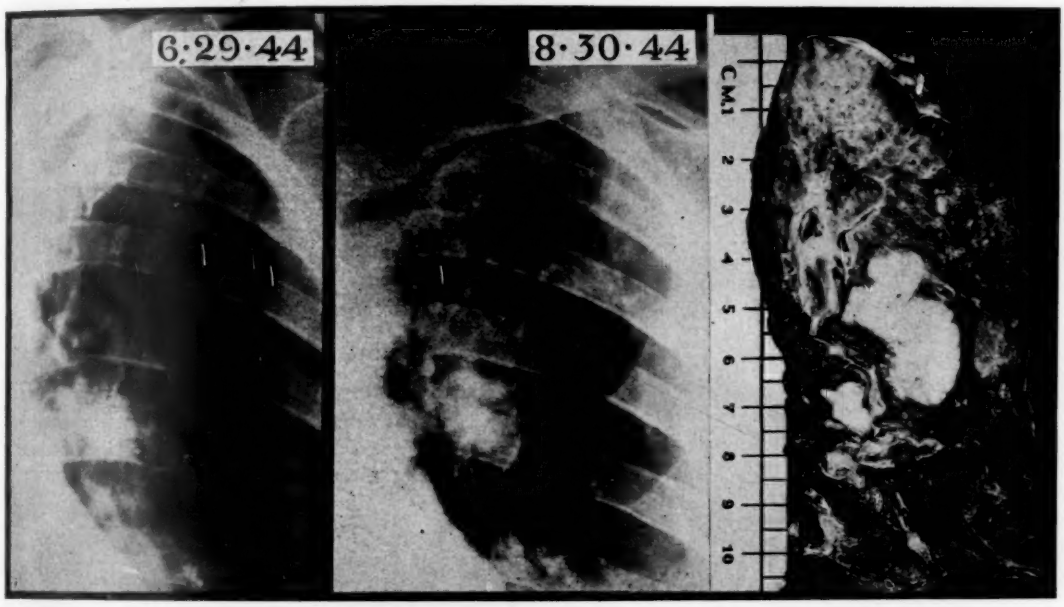

FIGURE 5. *Case 3085.*

This 52-year-old man was first seen on June 17, 1944, at which time he complained of a slight cough and expectoration, afternoon fever and an intermittent dull pain just below the angle of the left scapula. A chest roentgenogram (upper) revealed an area of increased density at the left hilum and an infiltration in the left upper lobe. Bronchoscopy was negative. Bronchiogenic carcinoma was suspected, and exploratory thoracotomy was about to be advised when the laboratory reported finding acid-fast bacilli in the sputum. The sputum was then cultured, and a guinea pig inoculated. These proved to be negative. A chest roentgenogram taken just before operation (middle) showed slight clearing of the infiltration in the left upper lobe. Exploratory thoracotomy was performed on September 1, and a tumor was found in the left upper lobe near the hilum. There were also considerable induration and suppuration of the lung tissue peripheral to the tumor. The surgical specimen (right) showed a large tumor (carcinoma, unclassified) near the hilum, as well as metastases to a bronchial lymph node. There was involvement of the parenchyma by infection distal to the tumor. Comment: *This case illustrates several interesting points. First, the symptoms were extremely mild. Second, the finding of acid-fast bacilli delayed exploratory thoracotomy, and if the laboratory report had been relied on, the patient might have been subjected to treatment for pulmonary tuberculosis. Third, the chest roentgenogram gave little evidence of the presence of the tumor itself, in spite of its size. In this respect it resembles Case 1268. The findings in these two cases emphasize the limitations of a routine posteroanterior roentgenogram. Stereoscopic, lateral and even oblique views should supplement the posteroanterior film in all cases with pulmonary disease. Finally, exploratory thoracotomy was the only diagnostic procedure that could possibly have established the diagnosis.*

sential facts. First, it is a safe procedure. Second, it is an efficient procedure and establishes the diagnosis in the vast majority of cases when cancer exists. Lastly, the diagnosis can be established at the operating table by frozen section, the operability determined, and the indicated operation carried out immediately.

Mediastinal Tumors

The problem of mediastinal tumors is one of increasing importance, for mass surveys show that they are much more frequent than has been suspected from previous clinical and autopsy data. The incidence of mediastinal masses in a recent survey conducted by the United States Public Health Service[11] was 0.012 per cent. Bloch and Tucker,[12] using routine fluoroscopic examination for all patients admitted to the University of Chicago clinics, found an incidence of mediastinal and diaphragmatic lesions of 0.57 per cent. When the large number involved in such surveys is considered, the magnitude of the problem becomes evident.

The mediastinum is the site of many different types of primary tumor, because of the varied types of tissue present and the complexity of embryologic development of the contained organs. From a pathological standpoint, mediastinal tumors present an extremely complex problem. The clinical approach and treatment are, however, fairly well standardized.

The problem with which we are now concerned is that of a patient whose mediastinal tumor has been discovered on the roentgenogram. The vast majority of those discovered in surveys cause either no symptoms or those so mild that they occasion little concern to the patient. The physician must answer two questions: what the nature of the mediastinal mass is, and how it is to be treated.

Localization is of the utmost importance in determining the type of tumor. The most frequent tumors of the posterior mediastinum are those arising from the sympathetic ganglions — ganglioneuromas — or the spinal nerves — neurofibromas. The tumors oftenest found in the anterior medi-

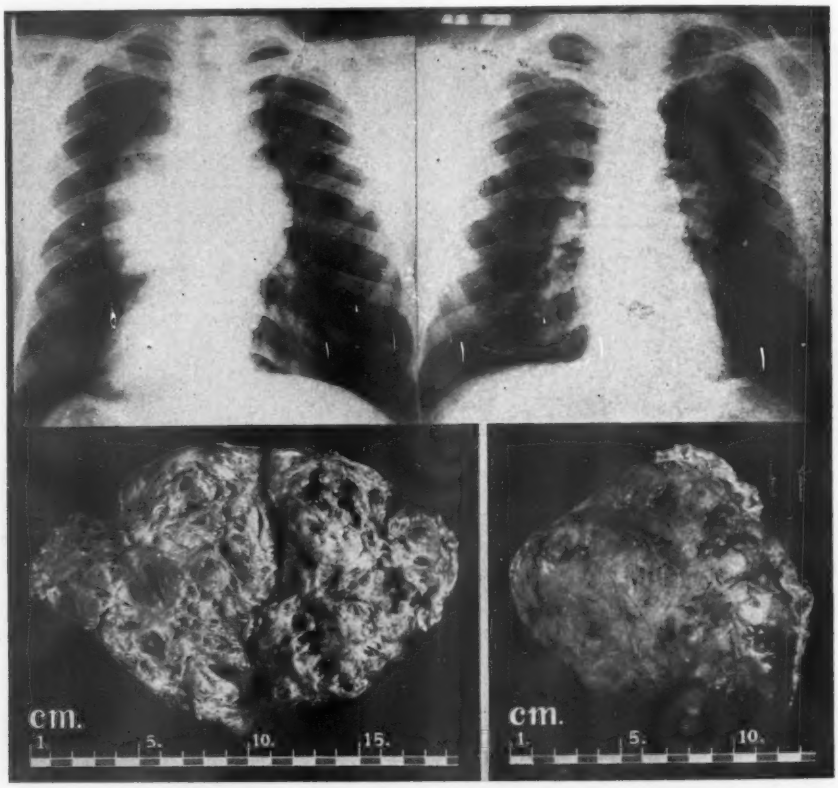

Figure 6. *Case 2704.*

This 20-year-old man received a medical discharge from the Marine Corps because of a mediastinal tumor that had been discovered in routine x-ray examination. He was in excellent health and entirely free of symptoms. The preoperative roentgenogram (upper left) showed a large mediastinal tumor protruding to the right and left of the mediastinum. Lateral views had shown that the tumor was in the anterior mediastinum. A preoperative diagnosis of a teratoma was made. The tumor was removed on December 9, 1943; the patient made an uneventful recovery and has remained well. A chest roentgenogram taken ten months following operation (upper right) was essentially normal. Examination of the surgical specimen (lower) proved the tumor to be an adenocystoma of respiratory epithelium. Comment: *This case illustrates the size to which a mediastinal tumor can grow and cause absolutely no symptoms.*

astinum are dermoid cysts, teratomas and malignant lymphomas, such as lymphosarcoma, Hodgkin's disease and leukemic lymphoma. It is therefore important to determine, if possible, whether the tumor is benign or malignant. The x-ray appearance helps to determine this. Benign tumors grow slowly and are usually oval or circular, quite dense, and sharply delimited laterally from the lung. Malignant tumors grow rapidly and are not so likely to be so smooth and discrete, but rather tend to be lobulated and less sharply defined from the pulmonary tissue. Cervical or axillary nodes are frequently associated with malignant lymphomas, and biopsy may prove the diagnosis. In case of doubt, a therapeutic test dose of x-ray helps to prove the nature of the tumor. Malignant lymphomas respond rapidly to x-ray therapy, whereas benign tumors are unaffected by it. In dermoids and teratomas, heavy-exposure roentgenograms with the Potter–Bucky diaphragm may reveal teeth or bone in the tumor. Fluoroscopy and roentgen-kymography assist in ruling out aneurysm.

Treatment

Statistics and experience show that the vast majority of benign mediastinal tumors eventually cause death because of malignant degeneration, infection or mechanical pressure on vital structures in the mediastinum. It is generally agreed that surgical extirpation is the proper treatment. Successful removal is the rule. The mortality is extremely low, especially if the operation is performed when the tumor is small and before any secondary changes have occurred.

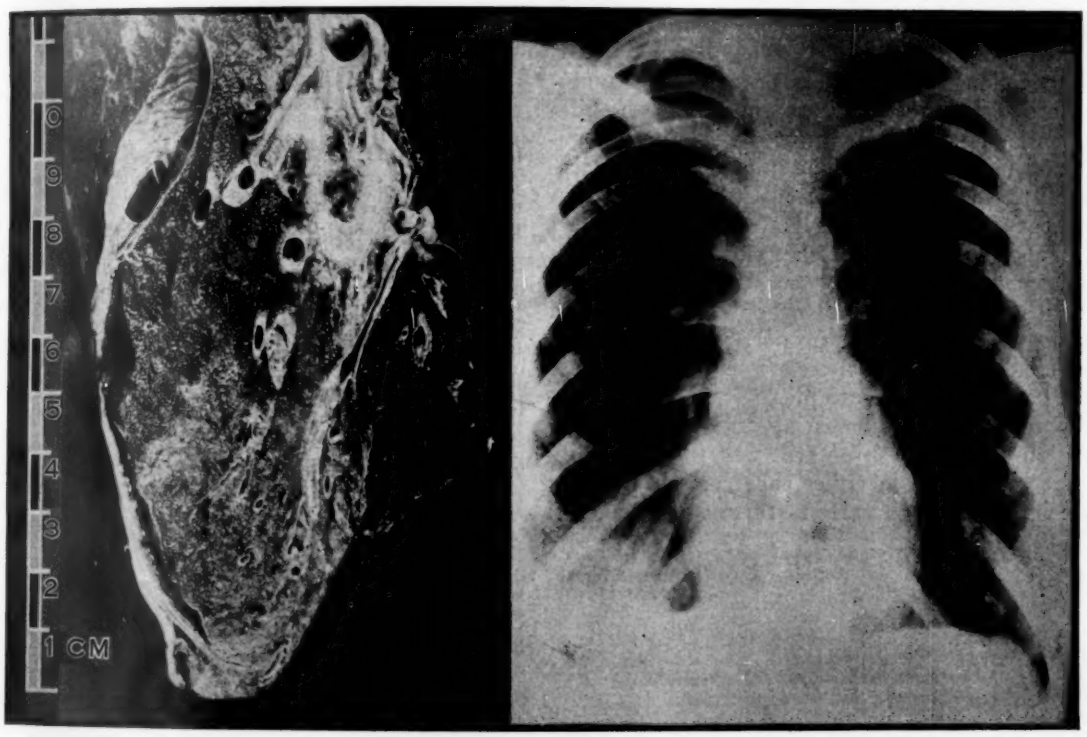

FIGURE 7. *Case 3301.*

This 34-year-old married woman applied in October, 1942, for a position in a hospital where a pre-employment physical examination, including an x-ray film of the chest, is routinely required. The survey film (right) showed an area of increased density at the right base. Bronchoscopy was immediately performed, and an early primary adenocarcinoma of the right main-stem bronchus was found. Before the end of the same month that the survey film was taken, the chest was explored and an operable lesion was found. The surgical specimen (left) showed adenocarcinoma of right lower lobe bronchus, with indurative pneumonia distal to the occlusion. The lymph nodes were negative. Convalescence was satisfactory, and the patient has remained free of symptoms. Comment: *This patient will probably be cured of a cancer for two reasons — first, because of the policy of one institution to require pre-employment chest x-ray films and, second, because of prompt investigation and treatment. If she had waited for symptoms to appear it might have been too late. If an explanation for the abnormal survey film had not been sought immediately it might have been too late. Fortunately for this patient the disease was apprehended when it was silent yet early, the potential danger of the lesion being fully appreciated.*

With these facts in mind, the treatment of mediastinal tumors can be expressed simply as follows. Surgical extirpation is indicated in benign tumors. An exception to this rule is a benign tumor in an elderly patient that is causing no symptoms. We advise frequent x-ray examination in such cases. So long as the tumor remains unchanged, no therapy is offered, but if it increases in size or causes symptoms, surgical removal is advised. In anterior mediastinal tumors, when there is doubt concerning the nature of the tumor, a therapeutic test dose

of x-ray is advised. If a response is noted, the tumor is considered to be a malignant lymphoma and x-ray therapy is continued. If the tumor fails to respond within four to six weeks, surgical exploration is advised. It is then important to proceed with excision without delay to avoid technical difficulties resulting from the effects of x-ray on local tissue.

Summary and Conclusions

Thousands of intrathoracic lesions are being discovered in mass x-ray surveys of the population. These patients are being referred to physicians in rapidly increasing numbers for evaluation and treatment.

Many lesions are in the early stage, when symptoms are either absent or so mild that the life-threatening lesion is unsuspected by both the patient and his physician. The immediate identification of the lesion and the institution of proper treatment during this stage offer the patient his best chance to get well. Delay may either rob him of an opportunity to have curative treatment or introduce factors that prolong or complicate such treatment. A significant proportion of all lesions discovered in survey work carry a definite threat to the patient's health and life.

A policy of watchful waiting until symptoms or extension forces the issue will not raise the percentage of salvages in either tuberculosis or cancer of the lung. The full value of survey work will not be realized unless a proper disposition of all uncovered lesions is made.

The medical profession is faced not only with the obligation but also with the privilege of evaluating chest disease in advance of the time when most patients ask for help — after progressive disease has caused symptoms. The potentialities of this type of preventive medicine are great. The profession has within its grasp the power to overcome the plague of tuberculosis and to tear the label of certain death from cancer of the lung.

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HOMOLOGOUS SERUM JAUNDICE FOLLOWING THE ADMINISTRATION OF COMMERCIAL POOLED PLASMA*

A Report of Eight Cases including One Fatality

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ALTHOUGH the occurrence of homologous serum jaundice has been repeatedly reported since 1937[1–14] the interest in this condition became widespread following its high incidence in American troops vaccinated against yellow fever in 1942.[15] The reports of Beeson[16] and others[10, 17, 18] gave evidence of the occurrence of the disease following transfusion with whole blood or plasma. A recent report by Rappaport[19] indicates that this sequela may not be infrequent in the armed forces. At present there are few reports of hepatitis in civilian hospitals following the administration of whole blood or plasma, although one might expect its occurrence to be frequent in view of the large amounts of plasma available for civilian distribution. In no reports have we seen any autopsy data, although such information in cases of hepatitis due to homologous serum used with immunizing agents has been recorded.[14, 20] The present report has been made to add to these data.

The discharge diagnoses of infectious hepatitis and catarrhal jaundice listed in the Northern Permanente Foundation Hospital files for September, 1943, to September, 1945, were reviewed with the object of separating all cases of homologous serum jaundice. Eight such cases appeared to satisfy the diagnostic criteria. One of these terminated fatally, and the autopsy findings are available for review.

It is recognized that any or all of these cases may represent a spontaneously occurring attack of infectious hepatitis. This criticism is, however, true of the other cases reported in the literature, since there are no specific diagnostic criteria distinguishing these two conditions at the time when the hepatitis is present, the clinical and laboratory findings being identical. The etiologic agents of the conditions have many capabilities in common, such as those of passing through bacterial filters, of surviving temperatures as high as 56°C. for a similar length of time and of being transmitted to new human hosts. Neither agent has successfully induced the disease in experimental animals, and the only known difference between them seems to be that relating to the incubation period. In homologous serum jaundice this is approximately fifty days to four months, whereas in infectious hepatitis it is usually less than fifty days. Another possible difference is that of ease of transmission, since the former is apparently more difficult to transmit by the oral and nasopharyngeal routes than the latter.[21–24]

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CASE REPORTS

CASE 1. E. P., a 31-year-old state highway patrolman, was admitted to the Orthopedic Service on March 14, 1945, and was operated on the same day for a simple fracture of the femur, with a Roger–Anderson pin fixation. He was given 250 cc. of plasma on the day of operation. On May 26, after running an irregular low-grade fever for 12 days, he developed generalized aching pains, anorexia, nausea and vomiting. Jaundice was noted clinically for the first time on May 30, at which time the icteric index was 55. It rose to 70 on June 4, and fell to 14 on June 21. By June 16, the patient was asymptomatic except for the fracture.

CASE 2. A. S., a 62-year-old engineer, was admitted to the Orthopedic Service on October 19, 1943, for a compound fracture of the tibia. He was operated on with the Roger–Anderson pin technic, and on the same day was given 250 cc. of plasma. He was discharged on November 6, but he was readmitted on January 22, 1944, with a history of epigastric distress, nausea and vomiting of 2 days' duration. The urine was dark and the stool was clay-colored. A tender liver edge was palpated on examination. The patient was obviously icteric, the index being 74. He was discharged asymptomatic on February 4, the icteric index having fallen to 41.

CASE 3. C. H., a 39-year-old rigger, was admitted to the Orthopedic Service on September 3, 1944, for a compound fracture of the left tibia and fibula. This was reduced by operation with the Roger–Anderson pin technic. On the day of admission he was given 250 cc. of plasma. Remanipulation of the fracture was done on September 25 and October 18. On October 20, anorexia developed. There was a brief episode of diarrhea at that time. On October 31, the icteric index was 26. By November 20, the icteric index was 84, but the patient was asymptomatic. By November 30, it had dropped to 25. There were no further symptoms.

CASE 4. M. N., a 27-year-old woman, a hospital employee, was admitted to the Gynecological Service on June 29, 1944, for perineal repair and a vaginal hysterectomy, at which time 250 cc. of plasma was given. Recovery was uneventful. On October 13, the patient was admitted to the Medical Service because of jaundice. She gave a history of epigastric distress and abdominal discomfort since October 1, dark urine, first noted on October 3, and clay-colored stools on October 13. The icteric index on October 14 was 66. The patient improved on symptomatic therapy and was discharged on October 27. On November 10, the icteric index was still 18.

CASE 5. M. W., a 23-year-old woman, a painter's helper, was admitted to the Medical Service on June 4, 1944, in diabetic coma. As part of her therapy she received 250 cc. of plasma. Recovery was uneventful, and she was discharged, but was readmitted on September 4 complaining of abdominal pain, diarrhea of 3 days' duration and nausea and vomiting for 1 day. She was obviously jaundiced, the icteric index being 50. She improved rapidly on symptomatic therapy. On September 18, the icteric index was 18.

CASE 6. A. B., a 39-year-old woman, a sheet metal worker, was admitted to the Medical Service on February 1, 1945, with lobar pneumonia and shock, for which she was given 250 cc. of plasma. She was discharged asymptomatic on February 7, but was readmitted on March 26 complaining of nausea and anorexia of 1 week's duration. On March 26, the icteric index was 48, the stools were clay-colored, and there was some bile in the urine. On April 11, the icteric index rose to 110. By April 16, it was 28. The patient was asymptomatic at that time and was discharged.

CASE 7. T. D., a 50-year-old shipwright, was admitted to the Medical Service on October 11, 1944, for pneumonia due to a Type 2 pneumococcus, with subsequent effusion. He had a history of duodenal ulcer. On October 11, he was given 250 cc. of plasma. On October 27, he was discharged asymptomatic. On February 22, he was readmitted because of gastrointestinal symptoms, which were attributed to the duodenal ulcer, and a subtotal gastrectomy was contemplated. On March 5, however, the icteric index was 35. The jaundice increased, and since the question of obstruction of the common duct was raised, exploration was performed on March 12. At operation the liver was slightly enlarged, pale and brown, without evidence of a metastatic lesion. The stomach was normal except for a small, firm mass with some scarring on the anterior surface of the pylorus. The head of the pancreas was indurated, and there was considerable edema of the surrounding tissues. The gall bladder appeared slightly edematous. The common duct and cystic duct were normal. At the time of operation the surgeon was unable to explain the symptomatology, and in view of the jaundice a subtotal resection was not done. The icteric index rose to 90 on March 14 and then gradually subsided. Following the operation, the gastrointestinal symptoms subsided, and the patient was discharged improved.

CASE 8. I. M., a 55-year-old sheet metal worker, was admitted to the Medical Service on March 13, 1945, for pneumonia of the right lower lobe due to Type 1 pneumococcus. He was given 250 cc. of plasma, in addition to the usual chemotherapeutic and supportive measures. After a rather stormy course, he improved considerably and was well on discharge on April 8. He was readmitted on May 5 with acute tonsillitis and evidence of a recurrence of the lobar pneumonia, and was treated for 5 days, with a prompt response to penicillin therapy. He was again readmitted on June 5, 1945. At that time he stated that he had had a shaking chill, muscular pain, weakness and a nonproductive cough of 2 days' duration. The temperature was 103°F. Physical examination was essentially negative. The white-cell count was 4300, with 62 per cent neutrophils. The urine was normal except for a slight trace of albumin. On June 8, jaundice was first noted clinically. The icteric index was 70 on June 9 and rose to 90 on June 11. The prothrombin time on June 11 was 6 minutes (control, 30 seconds). The patient became irrational on June 10, and then comatose. He went progressively downhill and expired on June 12 in spite of supportive therapy.

Autopsy. The organs were deeply jaundiced, and numerous subpleural and subepicardial petechial hemorrhages were found. The liver was of normal shape but was somewhat decreased in size, measuring 20 by 20 by 5 cm. Its surface was smooth and dark in color. It was pliable and flaccid, but cut with increased resistance. On the cut surface was seen a distinct pattern of dark-red dots and small lines on a greenish-ochre background. Several large, edematous periportal nodes were found. The spleen measured 14 by 9 by 4 cm. The capsule was tense and pale gray. On the cut surface the splenic parenchyma appeared deep red and congested and was firm, and the trabecular pattern was prominent. Malpighian corpuscles were not seen. The gall bladder was normal and contained some dark-green bile. Its ducts were patent.

Microscopically, sections of the liver showed the capsule to be intact. In large areas no liver cells were found. Those that remained were either in the periportal areas or at the periphery of the liver lobules. In place of the liver cells only the somewhat dilated capillaries remained. Numerous large, pigment-laden macrophages were scattered throughout the liver, and there was infiltration with lymphocytes and plasma cells and occasional polymorphonuclear leukocytes throughout the sections. The periportal areas contained dense accumulations of lymphocytes. Several sublobular veins were found that exhibited marked phlebitis. Their walls were infiltrated with inflammatory cells, which pushed the endothelium into the vessel lumen, and small areas of necrosis were seen. The bile ducts in the periportal spaces were of normal appearance and showed no attempt at regeneration. The liver cells, when preserved, were finely vacuolated and were undergoing necrosis. Very rarely, large liver cells or those containing two nuclei were found. Sections of the spleen showed distinct malpighian corpuscles. The pulp was deeply hyperemic. Sections of the lymph nodes revealed that all sinusoids were markedly dilated and contained large amounts of lymphocytes, plasma cells and polymorphonuclear leukocytes. The reticulum cells were somewhat increased.

The final anatomical diagnoses were acute necrosis of the liver and congestion of the spleen.

All these patients had negative histories with regard to drug or alcohol ingestion and exposure to toxic substances. X-ray examination of the abdomen was negative in every case. No patient had evidences of anemia.

DISCUSSION

It will be observed that these patients had incubation periods ranging from fifty-four to one hundred and thirty-nine days, which conforms with the incubation period of the experimentally induced disease. It should be noted that the patients in Cases 1 and 3 were in the hospital throughout the time between the administration of plasma and the development of hepatitis.

In no case was there known occurrence of hepatitis in any of the members of the patient's family, nor was there any known contact incidence in the hospital. Among the 77 cases of infectious hepatitis studied at this hospital in the same two-year period, 13 (17 per cent) members of the patient's family had or subsequently developed jaundice.

None of the patients were seriously ill except the one in Case 8. The autopsy findings in this case differed in no way from those in cases ending in death following hepatitis due to the administration of yellow-fever vaccine,[14, 20] nor are the findings different from those in deaths from infectious hepatitis.[25] In the absence of a biopsy, the operative report in Case 7 supplied no significant information, although the findings are not without interest.

During the two-year period during which these cases were observed, five hundred and one transfusions of commercial pooled plasma were administered. The plasma was purchased from a commercial manufacturer with nationwide distribution facilities, who states that each pool consists of at least fifty samples. The occurrence of 8 cases gives an incidence of 2 per cent, but this represents a minimal rather than a true incidence, since many patients received more than one transfusion and since patients who developed hepatitis were treated as outpatients or by physicians elsewhere did not come to our attention. Furthermore, patients who did not develop clinical jaundice but nevertheless had the clinical features of acute hepatitis, such as nausea, vomiting, anorexia and malaise, were not included. For example, we observed one patient with these symptoms and an icteric index of 13

ninety days after a transfusion of whole blood whose case suggests this possibility. Rappaport[19] has included 2 such cases in his report.

The true incidence of this condition is not known at the present time. Reports in the literature vary from as many as 26 of 47 cases receiving pooled serum in one instance[13] to ten thousand transfusions of pooled plasma without any recorded evidence of homologous serum jaundice,[26] although in the latter report the authors state that their method may not have supplied complete data. The reasons for this discrepancy are manifold. Since there is a relatively high incidence of infectious hepatitis at the present time, it is only natural to attribute any example of this clinical picture to spontaneously occurring agents. The long incubation period of homologous serum jaundice separates the disease from the etiologic event by such a long period that causal relation may be overlooked. Finally, many physicians may not be alert to this possibility because of the absence of information about this condition in the literature until the last few years.

The incidence of this disease is undoubtedly becoming greater because of the increased use of commercially pooled plasma in cases in which transfusion of whole blood from a single donor was formerly used. Our experience has confirmed this, since nearly one thousand whole-blood transfusions were given at this hospital in the same two-year period with no case of manifest jaundice. The chance of the etiologic agent's being given in any blood plasma therapy is many times increased as pools of fifty or more donors are mixed. The amount of icterogenic plasma necessary to contaminate a pool is minimal, since the disease can be transmitted by as little as 0.1 cc.[13, 21, 22]

In view of the disability[27] and the chance of fatality in homologous serum jaundice, the use of pooled plasma is not without danger. The fact that the icterogenic agent is not destroyed by drying and prolonged storage[23] makes the tracing of the icterogenic sample difficult. Since it has been reported that the agent is destroyed by ultraviolet radiation,[21] perhaps the hazard from the use of pooled plasma could be obviated by such a method.

Summary

Eight cases of hepatitis with jaundice following the use of commercial pooled plasma are presented, 1 of these being a fatal case, with autopsy data available.

The factors relating to the apparent incidence are briefly reviewed.

It is suggested that the hazard of hepatitis and even fatality from pooled plasma is greater than that of a whole-blood transfusion from a single donor.

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TYPHOID-BACILLUS INFECTION OF A SURGICAL WOUND: TREATMENT WITH A URETHANE-SULFANILAMIDE MIXTURE*

Report of a Case

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BOSTON

ALTHOUGH the occurrence of localized areas of suppuration caused by the typhoid bacillus is on the whole infrequent, McCrae[1] believes that during typhoid fever no part of the body in which abscesses may occur is exempt. *Eberthella typhosa* and pyogenic cocci, acting either alone or in combination, are the usual etiologic agents in this type of complication, which may occur without any apparent inciting cause, or as the result of injury to tissue by needle punctures, spontaneous hematomas or surgical procedures.

In most cases of abscess appearing in the course of typhoid fever, the lesions appear in various tissues without any apparent inciting cause. The buttocks are the most frequent site of abscess formation (McCrae[1]). Although localized areas of suppuration in the viscera are rare, spontaneously occurring abscesses of the thyroid gland, the cervical lymph nodes, the submaxillary glands, the breast (Sappington[2]), the spleen (Ransohoff and O'Rourke[3]), the ovary (Widal and Ravaut[4]), the rectus sheath (Bullowa[5]), the thigh muscles (Vires, Mas and Serre[6]), the muscles at the lower end of the sternum (Gannon[7]) and the peritoneal cavity, with or without perforation of the bowel, have been described. The reason for the focalization of typhoid bacilli in these various organs in typhoid fever in a particular patient is not apparent, but it seems most probable that during the stage of bacteremia organisms become located in these sites and, having established themselves, produce destruction of tissue.

Parenteral administration of various drugs has been incriminated in a number of cases as the cause for localization of typhoid bacilli in various muscles that have been used as sites of injection. Achard and Weil[8] have reported a case of abscess formation in muscle seven days after an injection of methylene blue in a patient with typhoid fever; aspirated pus yielded *E. typhosa* in pure culture. The intramuscular or subcutaneous administration of quinine (Schneider[9]), caffeine (Widal and Le Sourd[10] and Malenchini and Pieraccini[11]), oil of turpentine (Rathery and Bonnard[12]) and camphor (Tobias and D'Estefano[13]) has been reported as leading to formation of abscesses in some patients with typhoid fever; in most cases, the enteric organism causing the primary disease was isolated in pure culture from the localized area of suppuration. Tobias[14] who has recorded 2 cases of abscess formation due to the typhoid bacillus in typhoid-fever patients to whom camphor was administered parenterally, has expressed the opinion that such lesions when occurring during the acute course or convalescence of enteric fever are practically always due to *E. typhosa*. The pathogenesis of suppuration of this type appears to be mechanical irritation by the injected drug, with production of an area of decreased resistance and subsequent localization of organisms. Tobias could find no indication from his own cases or those reported in the literature that the appearance of an abscess has an unfavorable effect on typhoid fever; as a matter of fact, he expressed the opinion that in some cases the course of enteric fever is beneficially influenced by the development of a localized area of suppuration. Local injuries occurring without injections, such as hematomas in muscles, — which may result either from Zenker degeneration, which is sometimes present in typhoid fever, or from prolonged vomiting and coughing, affecting the abdominal muscles, — may serve to produce areas that are particularly susceptible to the establishment of the typhoid bacillus.

In spite of the fact that a moderate number of patients with typhoid fever develop complications requiring operative intervention, such as incision and drainage for osteomyelitis or laparotomy for intestinal hemorrhage or perforation, and that *E. typhosa* is capable of producing localized areas of infection, there is a scarcity of reports concerning suppurative complications of surgical wounds, a search of the literature having revealed only 2 such cases. Rathery and Bonnard[12] have described a case in which, following appendectomy because of pain in the right lower quadrant occurring at the onset of typhoid fever, the patient developed a superficial infection at the lower end of the operative wound, which, when incised and drained, yielded a pure culture of *E. typhosa*. A similar case of wound infection due to the typhoid bacillus following removal of the appendix in a patient who subsequently developed typhoid fever has been reported by Marta.[15]

The purpose of reporting the following case is to describe typhoid-bacillus infection in a surgical wound in the leg, without underlying osteomyelitis or periostitis, in a patient in whom the diagnosis

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of typhoid fever was first suspected on the basis of the bacteriologic findings in the local lesion; to point out the possible role of localized areas of suppuration in the spread of typhoid fever if, owing to lack of an exact bacteriologic diagnosis, proper precautionary measures are not taken; and to demonstrate the highly effective action of a mixture of urethane and sulfanilamide in the eradication of *E. typhosa* from a suppurated wound.

M.C., a 68-year-old married woman, was transferred to the Haynes Memorial Hospital from the Orthopedic Service of the Massachusetts Memorial Hospitals, to which she had been admitted on November 10, 1944, because of a fracture of the right femur sustained in a fall. She had enjoyed fairly good health until 3 weeks before admission to the Massachusetts Memorial Hospitals, at which time she had a mild febrile illness characterized by generalized aching and a low degree of fever. A physician made a diagnosis of an upper respiratory infection and recommended bed rest for several days. Recovery occurred without any further treatment, and the patient remained well until the fall, which resulted in an intratrochanteric fracture of the right femur.

Open reduction was carried out on the day of admission, and the bone ends were approximated by means of a Blount plate, with complete closure of the wound The course was uneventful until the 10th postoperative day, when there was a moderate elevation of temperature and the wound in the thigh appeared reddened, swollen and boggy and began to discharge purulent exudate. Cultures of the pus revealed *E. typhosa*. A macroscopic Widal test gave a positive reaction in a serum dilution of 1:320, both the organism isolated from the wound and a laboratory strain of the typhoid bacillus being used as antigens. Two subsequent cultures of the exudate from the wound taken during the next several days revealed the same organism. Because of these findings, the patient was transferred to the Haynes Memorial Hospital on December 6 for further care and treatment.

At physical examination on admission the temperature was 104°F., the pulse 90, the respirations 20, and the blood pressure 125/75. The patient appeared much older than her stated age. She was moderately well developed and poorly nourished, appeared chronically ill and was unable to give an adequate history because of an extremely poor memory. There were no rose spots or petechiae or a rash of any kind on the skin. The mucous membranes were pale and moist and showed no abnormal pigmentation or hemorrhagic areas. The posterior cervical and axillary lymph nodes were palpable, small, of normal consistence and nontender. There was no other lymphadenopathy. The pupils were equal in size and round and reacted to light and on accommodation. The scleras and conjunctivas were clear and of normal color. Examination of the eyegrounds revealed the disks to be of normal color, the margins well outlined and cupping of a normal degree. The retinal vessels showed narrowing, tortuosity and a moderate degree of arteriovenous nicking. No exudates or hemorrhages were seen. The right eardrum showed an old perforation, and the hearing was poor. The pharynx was clear and of normal color. The mouth showed no abnormalities except for absence of all but seven teeth, which were in poor condition. There was slight atrophy of the papillae of the tongue. The neck was not stiff, and there was no engorgement of the veins. The trachea was in the midline. The thyroid gland was not palpable. Examination of the chest revealed an increase in the anteroposterior diameter and equal expansion on both sides. Percussion over both lung fields was hyper-resonant, tactile and vocal fremitus were within normal limits, and the breath sounds were clear except for a few dry rales at the right base. Examination of the heart revealed a diffuse impulse in the 5th left interspace at the midclavicular line, a regular rhythm, distant sounds and a rate of 90 per minute. There was a Grade II rough, blowing systolic murmur, heard best over the aortic area and transmitted down over the precordium. The pulmonic second sound was greater than the aortic.

The abdomen revealed no spasm, masses or tenderness. The liver was palpable 2 or 3 fingerbreadths below the right costal margin. The spleen and kidneys were not palpable. No petechiae were noted on the abdominal wall. The genitalia were atrophic but revealed no other abnormalities. Examination of the extremities showed a well healed longitudinal scar 20 cm. in length on the lateral aspect of the right hip; in the center of this was a small sinus 1 cm. in depth, from which drained a small amount of thin, grayish, foul-smelling exudate. Palpation of the scar revealed no tenderness or masses. The extremities were otherwise normal except for moderate pitting edema of both ankles. Neurologic examination showed the deep and superficial reflexes to be physiologic. No abnormal reflexes could be demonstrated.

A specimen of urine taken on admission had a specific gravity of 1.014 and contained no albumin, sugar or abnormal cellular elements. During the hospital stay, the specific gravity varied from 1.009 to 1.032, the albumin from 0 to ++, on one occasion, and sugar was always absent. There were two episodes of pyuria, one in the 3rd and the other in the 7th week of the illness.

The red-cell count and hemoglobin were 3,910,000 and 10 gm., respectively, and remained at about these values during the hospital stay. The white-cell count was 6650, with 86 per cent neutrophils, 13 per cent lymphocytes, and 1 per cent eosinophils, and fluctuated thereafter between 4000 and 16,600, with essentially normal differential counts except on one occasion during the 2nd week, when 9 per cent eosinophils were present. The nonprotein nitrogen varied between 25 and 30 mg. per 100 cc. The serum calcium was 10.35 mg. per 100 cc., and the phosphorus 4.5 mg. The alkaline phosphatase level of the blood was 6 King–Armstrong units per 100 cc.

Cultures of the draining sinus in the right thigh made on admission revealed *E. typhosa* and a hemolytic *Staphylococcus aureus*. The gram-negative organism was again recovered 2 days later, but thereafter daily cultures of the wound, so long as it persisted, never again revealed the typhoid bacillus. On the 47th hospital day, 11 days after removal of the Blount plate, purulent exudate reappeared in the wound and bacteriologic studies revealed *Pseudomonas pyocyanea* in pure culture. This organism disappeared after 3 days of treatment. Further wound cultures were sterile.

Several cultures of the stool during the first 2 weeks in the hospital were negative for the typhoid bacillus, but in the 3rd week it was isolated. Five stool cultures made during the remaining 6 weeks were all positive for *E. typhosa*. Agglutinins against the typhoid bacillus, which had been present in a serum dilution of 1:320 on admission, rapidly increased, so that at the end of 2½ weeks they were detectable in a 1:1280 dilution.

X-ray examination of the chest revealed a few calcified mediastinal nodes and a network of increased density in both lungs, more marked on the right than on the left. There was no evidence of metastatic or primary neoplastic pulmonary disease. The right humerus showed an area of rarefaction made up of more or less round, pitlike areas measuring from 5 to 10 mm. in diameter, with sharply defined borders. Above this area was an amorphous calcification in the greater tuberosity. These findings were considered consistent with a small area of aseptic necrosis and were not thought to indicate neoplastic disease of the bone. Three roentgenologic examinations of the right femur at different times during the illness revealed no evidence of periostitis or osteomyelitis.

The temperature remained normal during the first 3 days in the hospital, fluctuated between 99 and 101°F. for the next week and gradually declined to within normal limits for the remainder of the hospital stay.

The volume of the sinus in the right thigh, as determined by the injection of sterile saline solution, was about 30 cc. After the causative agent of the infection in the operative wound had been identified, injection of 15 cc. of a sterile aqueous solution of 10 per cent urethane and 1 per cent sulfanilamide[15] into the sinus every 4 hours throughout the day and night was begun. Under this regimen, cultures of the wound for *E. typhosa* became negative in 36 hours and remained so during the remainder of the period of observation. The cavity decreased rapidly in size so that it was completely closed in 15 days. The quantity of urethane-sulfanilamide mixture injected daily was gradually diminished as the size of the sinus tract decreased, and treatment was stopped after 12 days.

On the 12th hospital day, the patient complained of a sudden attack of intense, knifelike pain in the right hip, which was relieved by rest but markedly aggravated by even slight

motion of the leg. Examination revealed an area of tenderness on the lateral aspect of the right hip. Lateral rotation or flexion of the right hip joint produced severe pain. There was no change in the appearance of the wound, no masses or tenderness could be elicited, and no exudate was present. The temperature and white-cell count were within normal limits. Morphine sulfate was administered and sandbags were applied to the leg to immobilize it. X-ray examination of the right femur revealed penetration of the head of the femur by the blade of the Blount plate, the point of which was lying in the joint space. Subsequent treatment by the application of Buck's extension and sedation produced complete relief of pain in 3 days. Twenty-four days later, the healed wound in the leg was reopened and the plate was removed. At operation, the bone was found to be completely united, the muscles and fasciae were in good condition, and nowhere was there any evidence of infection. Cultures taken from various sites in the operated area were sterile.

On the 11th day after operation, the wound opened spontaneously and discharged purulent exudate, from which *Ps. pyocyanea* was obtained in pure culture. The urethane-sulfanilamide mixture was applied every 4 hours to sterile dressings packed into the wound, and within 3 days the pigment-producing organism was absent; the purulent discharge ceased, and healing progressed so rapidly that the wound was completely closed 10 days after treatment was begun.

The hospital course was complicated by two episodes of pyuria, one in the 2nd hospital week and the other in the 7th. Bacteriologic study of the urine during the first bout revealed a pure culture of *E. typhosa*. Several subsequent urine cultures were sterile until the second attack of pyuria, at which time a pure culture of *Ps. pyocyanea* was isolated. Treatment with 2 gm. of sulfathiazole a day produced clearing of the urine in a short time.

Since the patient had become a typhoid carrier and required constant nursing attention because of her poor mental status, she was transferred to another hospital.

Discussion

There are several aspects of this case that merit detailed discussion. The original illness three weeks before fracture of the femur was in all probability an episode of extremely mild typhoid fever, which at its inception was mistaken for an upper respiratory infection, no effort being made to isolate the patient. Although the presence of *E. typhosa* in the urine and stool could well have been due to the carrier state, the rapidly rising agglutinin titer indicates active infection. Had the patient not incurred a fracture of the hip, with subsequent infection of the operative wound by the typhoid bacillus, the diagnosis of typhoid fever would in all probability never have been made.

The manner in which the enteric pathogenic bacteria gained entrance to the wound is open to conjecture. It seems probable that the organisms were not brought to the site of operation by the blood stream, since, if it is assumed that the original illness three weeks previously was typhoid fever, the bacteremic stage should have been over for an appreciable time. In the third week of typhoid fever, it is usual to find the organisms either in the stool or the urine or in both, and it seems most probable that the wound infection took place as a result of the introduction of organisms during or after operation through the skin of the thigh, which was contaminated either with fecal material or with urine. That the organisms did not enter the wound as a result of infection of the underlying bone or periosteum seems likely, since no roentgenographic evidence of osteomyelitis or periostitis was obtained. That there was a typhoid-bacillus abscess in the thigh muscles that was entered at the time of operation seems unlikely, since suppuration did not appear in the wound until ten days after surgical intervention. A remote possibility is that the organisms were present in the bone marrow without producing signs of osteomyelitis and were introduced into the wound during the procedure of inserting the Blount plate.

The similarity of the urine and wound cultures during the episodes of pyuria is of interest. When the wound was infected with *E. typhosa*, the same organism was isolated in the urine culture, and since there was marked pyuria, it seems proper to assume that the patient at that time had an acute pyelonephritis due to the typhoid bacillus. When, following the second operation, the wound became infected with *Ps. pyocyanea* and pyuria recurred, this organism was also cultured from the urine. These findings add some evidence in support of the possibility that infection of the wound resulted from contamination with bacteria that were present in the urine or the stool.

It has previously been demonstrated that *E. typhosa* is extremely susceptible to the action of urethane, large numbers of these bacteria being killed in the test tube by an exposure of five to ten minutes to a 10 per cent concentration of this drug in broth.[16] The bactericidal effect also appears to be exerted in vivo, since treatment of the wound described above with a mixture of 10 per cent urethane and 1 per cent sulfanilamide resulted in complete sterilization within thirty-six hours. *Ps. pyocyanea* has also been found to be highly susceptible to the action of urethane in vitro,[16] and this effect is apparently unaltered by the presence of tissue or exudate. This drug seems worthy of a trial in any localized infection with the typhoid bacillus, *Ps. pyocyanea* or other gram-negative organisms. It seems unlikely that the sulfanilamide in the mixture had any appreciable effect, since it is well recognized that the sulfonamides are relatively inefficient against gram-negative bacilli.

The danger of failure to recognize the presence of the typhoid bacillus in localized areas of suppuration should be stressed. If the diagnosis of typhoid fever is missed, as it may well be in extremely mild cases, such infected areas, which may be discharging a purulent exudate laden with *E. typhosa*, may be responsible for the transmission of the disease to other persons because of lack of proper precautionary measures. As a matter of fact, a patient who was in the ward at the same time as the one described above became ill with severe typhoid fever and, so far as could be ascertained, the case reported was the source of the infection. Rubenstein[17, 18] has stressed the importance of unrecognized typhoid-bacillus infection

in patients with acute or chronic cholecystitis who undergo surgical treatment as a source of spread of typhoid fever.

The possibility that wounds occurring during the course of typhoid fever, either accidentally or as the result of various therapeutic procedures, will become infected with the typhoid bacillus must always be kept in mind by those treating this disease. The possibility that these secondary lesions will act as sources for the spread of infection to susceptible persons must be carefully considered in the establishment of proper isolation technic. The rarity of reports of secondary infections of wounds with *E. typhosa* in patients who are operated on for the intestinal complications of typhoid fever is quite surprising, and it must be assumed that, on the whole, the resistance of skin and muscle to infection by the typhoid bacillus is high. A careful bacteriologic examination of all local areas of suppuration occurring in the course of typhoid fever is imperative.

Summary

A case of infection of a surgical wound with *Eberthella typhosa* in a patient who probably had an undetected mild attack of typhoid fever several weeks prior to operation for the open reduction of a fracture of the femur is described.

Treatment of the local infection with a solution containing 10 per cent urethane and 1 per cent sulfanilamide led to rapid eradication of the infecting bacteria and healing of the wound.

The importance of localized areas of suppuration due to *E. typhosa* cannot be overemphasized because, unless promptly recognized bacteriologically and the necessary precautions taken, spread of typhoid fever may occur.

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SYMPOSIUM ON MEDICAL SOCIOLOGY

MEDICAL PRACTICE AND ITS FUTURE*

LELAND S. MCKITTRICK, M.D.†

I UNDERSTAND that my place in this symposium is to tell you something of medical practice as it is today and something of its past, and to speak of those forces within and outside of medicine whose influences point toward the medical practice of tomorrow.

You are approaching the end of your medical-school training. Except for minor digressions, your thoughts and efforts have been on the scientific aspect of your chosen profession. What you may know of the actual practice of this profession cannot have come from personal experience.

Clinical medicine is not a science. It is the utilization of what we have learned from study and experience to determine and interpret the variable physiologic and anatomic responses of the body and mind to external or internal stimuli, and the application of this knowledge in such a manner that the proper treatment will be prescribed and will be accepted and carried out by the patient and his family.

THE DOCTOR

The practicing physician is the infantryman of the medical profession. To understand the practice of medicine, one must understand him; and this is not easy — especially for the nonprofessional person.

What are some of the outstanding characteristics of a good physician? A well developed intellectual curiosity, complete honesty, both moral and intellectual, and a devotion to his work that makes him available at all times of every day are some of the qualities that you have a right to expect in your doctor.

What are the factors that tend to develop and maintain in the physician the qualities that are so essential to good medical care of a community? I am not at all sure that I know the whole answer; but I believe that I do know at least a part of it. There are well recognized minimal requirements that medical schools must fulfill to give their students the minimum training essential to an adequate background for the practice of medicine. Schools that do not fulfill these requirements but accept medical students for training are of themselves inherently dishonest, and therefore cannot be expected to develop honesty in their students. A good school, a careful selection of students and the elimination of these found to be intellectually or morally unfit are, then, the first essentials.

The development of the proper emotional background of the doctor extends over a period of many years. Stimulated in the medical school, the young doctor has his most intensive exposure to the professional mind during his internship and in his association with the older men in the earlier stages of his entry into the actual practice of medicine. The practice in our teaching hospitals of holding staff meetings in which deaths, complications and errors are openly and frankly discussed exposes the young mind to a form of intellectual honesty not previously encountered. I thrill with pride each time one of our hospital residents voluntarily presents before the medical students and the staff a patient in whose management he has erred. By this action, he has accepted one of the basic principles of intellectual honesty; he has kept faith with himself, and has done what he could to prevent others from committing the same mistake.

Competition, both economic and professional, is an important and a most powerful influence. The practice of medicine to most doctors is their chosen way of making a living, and conversely, most doctors are dependent on their professional income for a livelihood. Every doctor knows that a satisfied and grateful patient is his greatest asset. You are rightfully told that if you can be a better doctor than your neighbor, are honest in your dealings with patients and are solicitous of their best interests, mentally and physically, you can be assured of a loyal and increasing group of patients and of satisfactory financial returns.

Every physician knows only too well of the patient's inability to distinguish what is good in medicine or surgery from what is bad. He knows, too, that there is no legislation or regulation that can adequately control the quality of medical or surgical care, except such regulations as are made by his professional associates. As a doctor, then, he not only has to satisfy the demands of his patients, but he must constantly strive to avoid any action that may receive the criticism of those professional associates, young or old, whose judgments he respects.

We hear much of the stimulus to do better work because of the personal relation between the doctor and the patient, and of the importance of the free

*This is the sixth of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January, February and March, 1945; they were sponsored by the Department of Preventive Medicine and were primarily intended for third-year students. These articles will temporarily replace the reports "Medical Progress."

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choice of a physician. There are many variations in the quality of medical care, not only within the same wards of our hospitals but even among patients under the care of a given member of the staff. We might not like to admit this, but if we are honest with ourselves, we shall realize that we are emotional human beings and that we respond to certain stimuli, just as do others who are differently trained. Later on in your daily work you will see patients under varying conditions — patients in the hospital wards who are merely the hosts of a given disease; the patient who may be referred to, not as Mrs. Jones, but "the woman in the corner bed with a cancer of the stomach." You will treat that patient's disease well. Later in the day you may go to your office and see a young mother with a similar condition. She tells you frankly that you operated on a relative or a friend of hers and that her doctor suggested the names of several surgeons, but that she came to you because she knew of you, and wanted you to operate on her if an operation was necessary. She expresses her confidence in you and her willingness to do whatever you advise, whenever you say it should be done, and she may well add, "I want to put myself completely in your hands." The quality of medical care that a given patient will receive from you as a doctor is dependent not only on your ability and experience but on the intensity with which you apply yourself to a given problem; and not infrequently it is this effort, over and above the average, that means the difference between life and death to the patient. Theoretically, all patients should get from the same doctor the same detailed care. Nevertheless, rightly or wrongly, the man who comes to you because he believes in you over and above anyone else is the patient who may well get from you that extra effort that represents the difference between the best you have to offer and just good medicine.

You may well feel that I have given too much time to the role of the individual, but the medical service of any community can be only so good as the doctors who are giving it. In any plan or discussion, therefore, that involves the relation between the doctor and society, there must be included a discussion of the quality of the service that is to be given, as well as the factors that influence its availability or its extension.

The Structure of Medical Practice

Various possibilities await the young man who has had a good training in his chosen branch of medicine. Time will only permit a limited discussion of the more significant of these.

A relatively small group of extra able, intense young men, whose great interest is in the teaching and advancement of the science of medicine rather than in the care of the patient, will go directly into full-time positions in large teaching hospitals. They will become the outstanding leaders in the medical education of tomorrow. On their shoulders will fall the responsibility for the scientific advancement of medicine and that of pointing the way to its clinical application. The importance and responsibilities of the subclinical branches of medicine, such as bacteriology, pathology and radiology, are now well recognized and attract an increasing number of young graduates. The great majority of young men and women, however, will go into clinical medicine, and for them there are a variety of opportunities. Many will return to their own homes or will go to their chosen communities as assistants to experienced and successful practitioners. This association is particularly valuable to the young surgeon.

Affiliation with an organized group, contract work in industry or simply starting a solo practice from scratch are some of the more usual openings. However interesting and instructive these first years may be, with but few exceptions they will not be productive from the financial point of view. They are considered to have been well spent if they permit a scant living but permit a continued opportunity to learn and to become acquainted in the community in which one expects to continue practice.

Probably the most difficult problem faces the young surgeon. In recent years it has been quite generally accepted that a minimum of five years after graduation is necessary for his training. By the end of this period he will have had an intensive exposure to surgical problems and will have become accomplished, although still relatively inexperienced, in the performance of surgical operations and in the care of surgical patients. The surgeon's confidence in himself, his ability to make decisions, and his technical skill, are rapidly lost, however, unless he can maintain a constant exposure to the problems of surgery and their solution.

Patients and referring physicians are slow in putting their confidence in a young surgeon, even though well trained. Moreover, the latter himself soon finds that whereas he has had an excellent training in the running of a surgical service and in the technical aspects of surgery, there are many practical problems involved in obtaining and maintaining the confidence of the patient, his family and the local physician that can be mastered only through experience under the conditions associated with the actual practice of surgery.

During this transition period, how is the young surgeon to maintain his technical skill while he acquires these other essentials necessary to his success? This question is immediately answered for those fortunate enough to obtain an association with a successful, experienced surgeon or with a group of surgeons, but for those not so fortunate this represents one of the major problems facing postwar medicine, and the answer is not yet at hand.

In summary, American medicine of today consists of fulltime research workers and teaching physicians; the fee-for-service doctors; the organized

clinics, either under the fee-for-service system, best exemplified by the Mayo, Crile and Lahey clinics, or the contract-service system, as offered by the Ross–Loos Clinic, of Los Angeles; and contract work, including insurance practice, such as has been in force in many parts of this country for the past half-century. In addition there are the subclinical branches of medicine so essential to modern practice.

Influences within the Medical Profession

Time will only permit the consideration of some of the more important forces within the profession that have influenced or are influencing medical practice in this country.

The American Medical Association

The American Medical Association was founded in 1847 "to promote the science and art of medicine and the betterment of public health." The *Journal of the American Medical Association* appeared in 1881, but neither it nor the Association was an active power in American medicine until the early part of the twentieth century. Membership is open to all legally registered physicians or graduates of qualified medical schools who have fulfilled the requirements of the local county medical society; in other words, membership in the latter automatically gives membership in the state and national organizations, with no additional dues or assessments for the latter. Members who subscribe to the official journal or one of its specialty journals become fellows of the Association. About 125,000 (approximately 70 per cent) of the physicians of this country are now members of the American Medical Association.

Although primarily educational in scope, the Association has a profound influence on medical practice. In recent years it has been much criticized for its conservatism, as expressed by its opposition to radical changes in the methods of medical practice. Although there is ample evidence that it has accepted certain changes, it is difficult to find anything to suggest an aggressive attitude on the part of the Association in favor of such changes, and it has violently opposed any alterations that are considered detrimental to the welfare of patients. There is, however, in the literature overwhelming evidence of its contribution to the advancement of the quality of medical education and medical care in this country. Only the briefest reference may be made to the more significant of these contributions.

In the early nineteen hundreds, through its Council on Medical Education and Hospitals, the Association was the most important single factor in setting and obtaining acceptance of the minimum standards of medical education and in eliminating a large number of so-called "diploma mills" and substandard medical schools. As a result of this, the number of medical schools in this country was reduced from one hundred and sixty-six to seventy-seven.

The American Medical Association is the central figure in the most comprehensive and effective system known for the perpetuation and exchange of medical information and opinion. The *Journal of the American Medical Association* is probably the foremost medical journal of the world. In addition, the Association has created and supports journals in many of the specialties, as well as the *Quarterly Cumulative Index* and *Hygeia*, a magazine for the laity.

The educational value of the annual meeting of the Association, with its scientific exhibit, is outstanding. The councils on Pharmacy and Chemistry, Foods and Nutrition, and Physical Medicine and the many committees appointed from time to time, such as the Committee on Cosmetics, the Committee on Contraceptives, the Committee on American Health Resorts and various committees appointed by sections, have helped to correlate scientific knowledge and to promote rational thinking in their respective fields, as well as to demonstrate that honest advertising is not only a moral obligation but is also consistent with profitable and satisfying material progress.

The Association's relentless campaign against quackery is well known. According to *Fortune*, this has resulted in the American Medical Association's being threatened with suits totaling $35,000,000 in the thirty years prior to 1938, of which only two ever came to trial, the total assessed damages amounting to just one cent.

It has fully co-operated with our government in the prosecution of the war, and is at present taking a leading part in plans for the guidance and postgraduate education of returning medical officers after the war.

Group Clinics

Fee-for-service system. The late nineties and the early nineteen hundreds saw in Rochester, Minnesota, the beginning of what was to become the best known group clinic in the world. As the years passed, the Mayo Clinic, under the guidance of Dr. Will and Dr. Charles, became the center of the best in medicine and surgery, and one of the best in scientific research and the training of physicians. Subsequent to this, there arose a large number of similar but smaller groups, particularly throughout the Middle West. Of all the many clinics that have developed, however, only three have reached national and international prominence. These are the Mayo Clinic, the Crile Clinic, of Cleveland, and the Lahey Clinic, of Boston. In addition to the excellence in the quality of medicine provided, these clinics have one common and apparently essential factor: the presence of an unusually able and dynamic leader — in each case a surgeon — who has excelled not only professionally but in the organization, selection and

the management of personnel necessary to the success of the undertaking.

Contract-service system. In 1929, Dr. Donald E. Ross and Dr. H. Clifford Loos, of Los Angeles, were approached by members of the Department of Water and Power of that city concerning the possibility of organizing for them a medical service, financed through periodic payments. With this stimulus, the Ross-Loos Clinic group was formed and began to function on April 1, 1929. For a monthly fee of $1.50 — later raised to $2.00 — for each subscriber, the group agreed to provide medical service, including attention either from a general practitioner or a specialist in the central offices or the hospital, or in the subscriber's home if the patient was unable to come to the clinic. Subscribers were to receive laboratory and x-ray services, physical therapy, ambulance service, drugs, dressings and hospitalization in a ward bed. Additional charges were made for certain services, such as dental work, special drugs and appliances.

In 1934, Dr. Ross and Dr. Loos were expelled from the Los Angeles County Medical Society, not because the clinic was engaged in contract practice but because it was alleged that there was a solicitation of patients. The expulsion was sustained by the California Medical Association, which automatically brought suspension from the American Medical Association. According to the constitution of the latter, such expulsion is subject to appeal before the Judicial Council. This appeal was made, and on January 2, 1936, the action of the county and state societies was overruled. The conclusions reached by the Judicial Council were as follows:

> *a.* The appellants were brought to trial with no definite knowledge of what they were charged.
> *b.* There was no adequate opportunity to defend themselves.
> *c.* They were expelled for some unknown act not appearing in the charges.
> *d.* They did not have a fair trial.

Following this action by the Judicial Council, the two physicians were reinstated by the county medical society.

At the present writing there are one hundred and ten full-time doctors of medicine in the group, all of whom are members of the county medical society and therefore of the American Medical Association. Dr. Loos is a member of the House of Delegates of the California Medical Association and holds an important chairmanship in the local society; indeed, it is said that a most cordial relation exists between the physicians of the clinic and other doctors in the area. The clinic provides service for about 110,000 people in the Los Angeles area. The cost to the subscriber is $2.50 a month. Dependents of subscribers are not included in this fee, but are accorded care at special rates — for example, office consultation or treatment, 75 cents; refraction, $1.00; residence calls, daytimes, $1.50, and nights (between 9:00 p.m. and 8:00 a.m.), $2.00; minor operations, $15.00; and major operations, $25.00.

The above group and others similarly organized and controlled maintain excellent standards of medical service. Unfortunately, there developed in many communities groups supposedly organized on the same basis but actually organized by lay promoters, patronage being secured by advertising and solicitation. Where such organizations have developed, competition for patronage has resulted in a reduction of premiums and a lowering of the quality of medical care. In one state one hundred and forty-three such organizations were promoted as medical-service plans, with lay promoters acting as medical brokers and in some instances contracting with clinics or private groups of physicians in hospitals for the services promised to the prospective patient. In other groups no medical contracts were made and therefore no medical services were available to the enrolled members.

Nonprofit Prepayment Hospital-Service and Medical-Service Plans (Blue Cross and Blue Shield)

"Back in 1929, when Baylor had an idea that hospital costs could best be borne by group action, a budget plan for meeting certain but unpredictable hospital bills was established." This quotation is from a letter written in August, 1944, by Lawrence Paine, administrator of Baylor University Hospital, of Dallas, Texas, and gives the beginning of what has become known as the Blue Cross program. Group Hospital Service, Incorporated, of Dallas, was inaugurated on a statewide basis in 1939 and experienced a phenomenal growth, but two years later was confronted with a deficit of $110,000. Then followed a period of readjustment, and one year later Group Hospital Service was pronounced financially sound.

The Blue Cross program, as it has come to be known, was designed to cover the cost of hospitalization for patients in the lower-income groups who went into hospitals at so-called "semiprivate" accommodations. It covers either individuals or families, and usually includes all the ordinary costs payable to the hospital for a given period of time, generally three weeks. Persons must join in groups. The organization is on a nonprofit basis, and the cost for its protection is about 85 cents a month for an individual and $2.00 for family membership. At the present time approximately 18,000,000 persons in this country subscribe to the program.

In addition to the Blue Cross program there are medical-service plans, most of them sponsored by the medical societies of various states. One of the largest and most successful of these is Michigan Medical Service, which was organized on a statewide basis by the Michigan State Medical Society in 1940. When first established, it gave, in conjunction with Michigan Hospital Service, complete hospital, medical and surgical services to subscribers

and their families. There is no income limitation on eligibility to enroll, but if the income of an unmarried subscriber is more than $2000 or that of a married one is more than $2500, the amounts allowed may not be adequate to cover the entire professional fee. In 1942, the Michigan Medical Service had to discontinue its medical coverage in favor of surgical coverage only. There is ample actuarial experience for the successful establishment of a surgical plan. The problems involved in sound actuarial medical plans have, however, not yet been satisfactorily solved, although all plans look forward to the inclusion of medical services as increasing experience permits. To us in Massachusetts, it is encouraging to learn that in the first quarter of 1945 the Massachusetts Medical Service — established by the Massachusetts Medical Society — had the largest net enrollment of any medical society plan in the country, and that in the near future it anticipates the inclusion of medical care in the hospital without an increase in rates.

In addition to the Blue Cross and Blue Shield programs, a large number of projects under the stimulus and guidance of medical groups are being put into practice throughout the country. Thus, the State Medical Society of Wisconsin is actively working at the present time on a plan to provide complete coverage to low-income groups throughout the entire state.

Medical Committees

The Committee of Physicians for the Improvement of Medical Care, Incorporated. This committee was formed in 1937 by a small but well known group of physicians, many of them in the field of medical education. They believe that "the health of the people is a direct concern of the Government." This committee has taken an active part in an attempt to outline the principles of an improved medical practice. Its communications have been few but dignified and constructive, although many times not in agreement with current medical thought. Its letter of congratulation to Senator Wagner after the introduction of his bill (S. 1161) suggests that the committee was willing at that time to favor the adoption of a compulsory federal health system.

The National Physicians Committee for the Extension of Medical Service. This committee was established in 1939. Most if not all of its members, too, are well known in medical circles, although they are more representative of medical practice than of medical education. This committee has no direct affiliation or working connection with the American Medical Association, but its principles have been endorsed by the House of Delegates of the Association and active in its work are some who are or have been actively interested in the American Medical Association. The National Physicians Committee believes that the necessary and desirable steps to improve and spread the cost of medical care can best be done within the framework of principles approved by the medical profession. It favors state and local rather than federal subsidies to the indigent. The committee has been criticized for its violent attack on the Murray–Wagner–Dingell Bill. Its widely heralded opposition to S. 1161 and the committee-sponsored polls by the Opinion Research Corporation, of Princeton, New Jersey, have, however, undoubtedly done much to awaken the medical profession of the country to the need of taking an active part in developing or recognizing an improved medical practice more acceptable to the public who pays for it.

Influences Outside the Medical Profession

Group Insurance for Industrial Workers

In 1912, Montgomery Ward and Company, of Chicago, purchased from an insurance company a group-insurance policy. This provided life insurance for all employees and is said to be the first group life-insurance policy written by any private carrier in this country.

For over twenty-five years, the Endicott–Johnson Shoe Company, of Binghamton, New York, has provided full medical care and hospitalization for all workers and their dependents, without cost. Between that time and the present, there has developed an increasing interest on the part of industry in the type of medical care given to employees and their dependents, and in 1943, according to a recent survey of the National Physicians Committee, there was a total of nonduplicated insurance — including the Blue Cross — in this country covering more than 25,000,000 persons. The coverage in the various policies varies tremendously, as does the proportion of the cost paid by the worker and by the employer. It has been suggested that complete group health insurance might consist of the following: for employees, life insurance, equal to approximate annual earnings, sickness benefits equal to 25 to 50 per cent of the weekly wage, hospitalization from $4 to $7 a day, hospital extras from $20 to $35 for each illness, surgical care on the basis of a fee schedule (maximum, $150), medical care with a fixed maximum benefit and a retirement annuity based on service earnings; and for dependents, identical coverage for hospitalization and surgical and medical care.

There are, however, definite weaknesses in each of the group policies now available through private companies. Outstanding among these weaknesses are the facts that too large a group is required to obtain minimum costs and that insurance protection may be forfeited when employment ceases.

Outstanding in its accomplishments is the highly successful prepaid medical plan that has been set up by Dr. Sidney Garfield at the direction of Mr. Kaiser for his shipbuilders in California (Southern Permanente Foundation) and Washington (North-

ern Permanente Foundation). In the Oakland, California, plant, 62,000 of the workers (90 per cent) have joined the plan, which is voluntary. Excellent and complete care is given in their own hospitals. Because of war-time limitations, the families of the workers are not included. The organization works in complete harmony with the local medical profession.

Group Health Association, Incorporated

This association was granted a charter in Washington, D. C., in February, 1937, with an appropriation of $40,000 from the Home Owners' Loan Corporation. Through a staff of hired physicians, it proposed to offer to federal employees and their families most types of medical and surgical care at a stated annual cost. The Medical Society of the District of Columbia opposed this scheme, believing that it was not to the best interests of the public or the physician and was in violation of its code of ethics. According to an article that appeared in the *Journal of the American Medical Association* just before the Group Health Association began to function actively, it was thought that the organization was practicing medicine illegally and that the physicians employed were primarily the agents of the association and not those of the patients and that since the bylaws provide that the medical director shall render such reports as the Board of Trustees shall require, all privacy and secrecy between physician and patients would be destroyed. It was also held that there was no opportunity for the freedom of choice of his physician by the patient. One of the members of the Medical Society of the District of Columbia was therefore expelled, and several other physicians resigned from the association. Following this, the American Medical Association and others were indicted by the Department of Justice and were convicted of violating the Sherman Anti-Trust Act. This conviction was upheld by the United States Supreme Court.

Proposed Changes

Murray–Wagner–Dingell Bill

On June 3, 1943, Senator Wagner — for himself and Senator Murray — presented a bill (S. 1161) framed to broaden the present Social Security Act. It included a provision for medical care supported through payroll deductions for the employed and direct taxation for the self-employed.

According to the committee appointed by the American Bar Association to study and report on this bill, its authors are Isadore S. Falk and Wilbur J. Cohen, director and assistant director, respectively, of the Bureau of Research and Statistics of the Social Security Board, and Philip Levy, secretary to Senator Wagner. It may therefore be assumed to represent the opinion of the Social Security group concerning the manner in which the health of the country can be best protected. It provides complete medical and hospital care for approximately 110,000,000 persons. It provides for an advisory health council to be appointed by the Surgeon General of the United States Public Health Service, whose members are authorized to advise him with reference to carrying out the provisions of the act. It provides aid for research and for undergraduate and postgraduate education. It puts complete responsibility for carrying out its provisions on the Surgeon General.

The bill met with violent opposition from many quarters — the American Medical Association, the National Physicians Committee, the American Bar Association, most business organizations and many others who saw in it the centralization of medicine as the initial step toward more complete centralization of all American activities. Organized labor, the National Farmers Union and most social workers favored its passage. It has not been and probably will not be reported from committee.

Pepper Committee Report

The Senate Subcommittee on Wartime Health and Education, with Senator Claude Pepper as chairman, has recently reported on the investigation by this committee of the health of the Nation. It emphasizes that its findings are preliminary. It recommends that federal grants-in-aid be made to the states for the construction of hospitals, medical centers and health centers, in accordance with integrated states' plans approved by the United States Public Health Service. It reports an acute shortage of personnel with training in psychology and psychiatry and points out the need of increasing such personnel. It recommends that federal scholarships or loans be made available to qualified students, and urges an increased enrollment of women in medicine, dentistry and so forth. It makes no specific recommendations in regard to health insurance, but points out the importance of group financing. The report states:

> Any method which is evolved should offer complete medical care, should be reasonably but not "cut rate" in cost, should include substantially all of the people, should afford the highest quality of care, should permit free choice of physicians or groups of physicians, should allow democratic participation in policy making by consumer and producers, should be adaptable to local conditions and needs, and should provide for continuous experimentation and improvement.

The report is well written and suggests that the work and recommendations of this committee should be carefully followed by all those interested in the future of medical practice.

* * *

In closing, let me remind you that the practice of medicine as you will know it may differ in many ways from that which we know today. There are many forces at work both within and outside medicine to give all the people of this country the best possible medical care at a cost within their

reach. There is common acceptance of this objective, but there are widely divergent views concerning the best methods of attaining it. I shall only add that the actual care received by a given patient will always depend on the character and ability of the individual physician, the quality of his training in school and during the early years after graduation the conditions under which he practices, and the opportunities and incentives for continued educational advancement, and that any changes in medical practice that do not have as their primary objective a continued improvement in the quality of service given may well lower rather than elevate the standard of health of the American people.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

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CASE 32061

PRESENTATION OF CASE

A fifty-year-old theater manager entered the hospital complaining of vomiting of blood.

Five months before admission he felt nauseated and vomited a large blood clot. After this episode he felt well until six weeks later, when he again experienced severe nausea and vomited a large quantity of blood. During the following three days he had four more massive hematemeses, with tarry stools. He had received several blood transfusions.

The past history revealed that for years the patient had complained of upper abdominal pain, gaseous eructations and nausea. At the age of thirty-five an exploratory laparotomy because of continued discomfort revealed a "bulbous growth on the appendix," and an appendectomy was performed. Twelve years before admission the patient had five pleural effusions in one year and was sent to a sanatorium for eleven months. For about one and a half years after discharge he had no pain. Ten years before admission, attacks of severe epigastric pain, nausea and flatulence began. They were not related to meals, frequently occurring at night. The pain usually began in the right costovertebral angle but then spread anteriorly over the right upper quadrant, with some radiation across the left side and toward the back. The pain was not relieved by alkalis or a bland diet but was always relieved by vomiting. Two years before admission a gastric aspiration revealed acid-fast bacilli. He again went to a sanatorium, where the sputum and gastric juice were each positive on one occasion. During the fifteen months before admission the gastric juice was negative for acid-fast bacilli.

Physical examination revealed the patient to be well developed and nourished and in no distress. The heart, lungs and abdomen were normal.

The temperature was 97.4°F., the pulse 82, and the respirations 18. The blood pressure was 108 systolic, 70 diastolic.

The red-cell count was 4,860,000, with 14.3 gm. of hemoglobin. The white-cell count was 12,700. The urine was normal, as were the blood chemical findings. Gastric analysis revealed 5 units of free hydrochloric acid in the first specimen, 15 units in the second and 79 units in the third. The gastric juice was guaiac negative and contained no acid-fast bacilli by the alum flocculation method.

A gastrointestinal series showed no evidence of esophageal varices or of hiatus hernia. The stomach was normal in form and function. Barium passed the pylorus without delay, filling the duodenal bulb to a normal contour. The tip of the bulb, however, was consistently deformed, especially when the bulb was collapsed. A definite ulcer crater could not be found. Barium passed rapidly through the small bowel. A barium enema was essentially negative.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. LELAND S. MCKITTRICK: Before seeing the x-ray films we might summarize this story. This man began to bleed five months before admission, vomiting a little blood. Six weeks later he had recurrent, apparently massive, hemorrhages over a period of three days. He vomited blood, and he passed bloody stools. He had several blood transfusions. Although it does not so state, I presume that it is fair to assume that he had had no bleeding for approximately three and a half months. In the past he had had a good deal of abdominal pain, which to me is indefinite in character and means nothing so far as pointing to a diagnosis is concerned. It was not characteristic of a duodenal ulcer or of gallstones; indeed, it was not characteristic of anything and means nothing to me at the moment. This man had acid-fast bacilli in the sputum. I presume that tuberculosis alone would not be adequate for a diagnosis. I do not believe, however, that we should spend more time on it; it probably does not enter into our problem, since we do not have to decide whether the patient should be operated on. I think we can safely assume that the blood came from the upper gastrointestinal tract and not from the bronchial tree.

Dr. Milford D. Schulz: Then I shall just tuck this x-ray film of the chest down in the corner.

Dr. McKittrick: I am constantly looking with great expectation to the day when the radiologist helps me at this stage of the game.

Dr. Schulz: I do not believe that this is the time. These are the films of the colon, made on two successive days. The second examination was made because of a defect seen near the splenic flexure. It is no longer evident on the second examination. These are films of the lower esophagus, and they show no evidence of varices. The stomach is quite normal in appearance. The only thing seen is the deformity of the distal portion of the duodenal bulb, but there is no evidence of an active ulcer crater. The duodenal loop is entirely normal in appearance. There is nothing abnormal in the appearance of the small bowel.

Dr. McKittrick: Thank you, sir. I continue to appreciate your efforts.

I might say right now that I am not going to make a diagnosis because I do not know what this man had. The blood that he vomited probably came from the stomach or duodenum. I say that simply because we have no evidence that it could have come from any place else. There were no symptoms or evidence suggestive of anything in the esophagus: he did not have varices demonstrable by x-ray, and no hiatus hernia. Without symptoms referable to the esophagus and without evidence of a lesion of the esophagus by x-ray, the esophagus is out of the picture so far as I am concerned. We know that the blood could not have come from a site much lower than the duodenum because most of it was vomited. Therefore, we are not concerned with anything below the level of the duodenum. That narrows the field to the stomach and the duodenum, and there is something more than the fact that this is a conference case that makes me suspicious that what the x-ray films show was not the cause of this man's bleeding. This is only a suspicion because there is nothing definite to go on.

The patient had vomited blood with blood clots on one occasion. Possibly that is more suggestive of the stomach than the duodenum, but I am not sure of it. I completely distrust his story so far as it has anything to do with the present situation. The bleeding might have been due to a duodenal ulcer, or it might not. There is, as you know, a lesion sometimes called duodenal ulcer occulta, an ulcer in the second portion of the duodenum in the region of the ampulla. The symptoms in such cases are indefinite, the patient may be operated on for almost anything except duodenal ulcer, and the ulcer is apt to be missed at operation unless the surgeon is particularly on the alert. This may be one of these cases, but I doubt it. We do not have the benefit of x-ray examination promptly after the hemorrhage. Careful x-ray study at such a time is particularly useful.

It has been my very limited experience that when I am not able definitely to demonstrate from the clinical evidence the source of a man's bleeding I am apt to be disappointed at operation. A gastroscopy was not done. I do not know of any reason why it should have been done. I presume that if this man had active gastritis it probably would have shown by x-ray examination, although all the acute episodes happened three and a half months before entry. Since I have to make a diagnosis, I shall have to call the lesion a duodenal ulcer because of the deformity shown at x-ray examination, but I shall quickly add that this is probably wrong. I am strongly suspicious that the bleeding came from the stomach. If it came from the stomach it could have been caused by any one of a number of things, including an ulcer or gastritis that had healed; I believe it was likelier due to a lesion that was missed by x-ray examination. Even the X-ray Department does occasionally miss a definite lesion of the stomach. I do not believe, however, that it often misses an ulcer or a carcinoma, but something like a leiomyoma is sometimes difficult to spot, particularly if it is small. I have to leave it at that.

I will say that this man had a healed duodenal ulcer, but I am suspicious that tucked away in the stomach some place there was a lesion from which this man bled.

Dr. Tracy B. Mallory: Are there any other suggestions?

A Physician: Was this man an alcoholic?

Dr. Gordon A. Donaldson: No.

Dr. Mallory: Will you tell us about the operative findings, Dr. Donaldson?

Dr. Donaldson: We were just as unhappy about the diagnosis as Dr. McKittrick is. There were many points in favor of a duodenal ulcer. We thought that the bleeding was typical of the upper gastrointestinal tract; and this patient was a perfect type for an ulcer, since he was a thin, asthenic, theatrical manager, with a high gastric acidity.

We were also interested in the upper abdominal cramps, which he had had for years, and at operation, Dr. Allen carefully explored the ileocecal region. The vessels over the serosa were definitely dilated, but the bowel wall seemed to be essentially normal. We thought that the bleeding could not have come from that source. There was an avascular adhesion between the gall bladder and the duodenum, which was cut, and the duodenum was thoroughly explored without finding any evidence of induration or ulceration. He then turned his attention to the stomach itself, and while he was exploring the mesenteric border, high on the lesser curvature, the cause of the bleeding was found.

Clinical Diagnosis

Duodenal ulcer.

Dr. McKittrick's Diagnosis

Duodenal ulcer.

Anatomical Diagnosis

Neurinoma of stomach.

Pathological Discussion

Dr. Mallory: This was a tumor of the stomach wall. It projected only externally from the muscle layer, which explains the failure of the X-ray Department to visualize it. There was a slight crater — a shallow ulceration of the mucosa just over the tumor. If that had been caught in a certain plane, it might have been demonstrable.

The tumor was of the spindle-cell type, which pathologists usually argue about — whether it is a leiomyoma or tumor of nerve-sheath origin. We classified this as a neurinoma, which is, in my opinion, the more frequent of the two tumors in the stomach. It was slowly growing and can safely be called benign. There is not much doubt that the man is cured.

CASE 32062

Presentation of Case

A fifty-year-old pipefitter was admitted to the hospital complaining of substernal pain.

One hour before admission he was doing his regular work at the Navy Yard but exerting himself more than usual. He was suddenly overcome by a sensation of heavy substernal compression. He felt weak and sat down. He was taken to the Infirmary, where he was given 16 mg. of morphine sulfate. He was then brought to the Emergency Ward, where he complained of substernal pain radiating to both scapulas.

The past history revealed that a year before admission the patient was treated at another hospital for olecranon bursitis. At that time the blood pressure was not recorded. The heart was not enlarged, and the pulse was 70 and regular. There were no cardiac murmurs. A Kahn test was negative. Twelve years before admission he was found to have a systolic blood pressure of 185, which decreased after treatment. Eighteen years before admission he was treated for a urethral stricture, but he denied venereal disease. At no time had there been any evidence of cardiac failure.

Physical examination revealed the patient to be apprehensive and pale. He was not dyspneic. The skin was moist. The heart was enlarged to the left, but the border was difficult to percuss. Extrasystoles were frequent, with occasional runs of eight or more. A Grade I systolic murmur and a Grade II diastolic murmur were heard at the apex. At the base, over the sternum, was heard a Grade III to-and-fro murmur, loudest in diastole. There were no thrills, and no carotid transmission. The lungs and abdomen were normal. There was no ankle edema.

The temperature was 98°F., the pulse 84, and the respirations 20. The blood pressure was 160 systolic; 100 diastolic.

The red-cell count was 5,300,000, with 14.5 gm. of hemoglobin. The white-cell count was 13,400, with 87 per cent neutrophils. The urine gave a ++ test for albumin, and the sediment contained an occasional white cell.

An x-ray film of the chest taken on the first hospital day showed an area of increased density lateral to the apex of the heart and in the cardiophrenic angle. Above this, at the level of the left hilus, there was a linear shadow of increased density. The aorta was rather tortuous. Another film, taken on the second hospital day, showed a similar picture, with a small area of hazy density at the left base. A third film, taken on the day before death, showed that this area had almost completely disappeared. An electrocardiogram showed normal rhythm, with a rate of 100. Evidence of left-axis deviation was present. The PR interval was 0.15 second. There were many premature beats in Leads 1 to 2 that originated from varying ventricular foci. The T waves were upright in Leads 1 and 2 and in the precordial lead but flat in Lead 3. QRS, was slurred. There was a run of ventricular tachycardia in CF_5.

Soon after admission 0.2 gm. of quinidine sulfate was ordered every four hours. Ten hours after admission, the patient was much improved, sleeping well and exhibiting a much more regular cardiac rhythm. The extrasystoles, however, persisted. He complained of no pain. On the second hospital day the left calf was noted to be tender, and the right swollen. The temperature rose to 105°F. He complained of pain in the left chest on respiration, and bloody sputum was noted. The breath sounds were diminished over the left lower lobe. A bilateral femoral-vein ligation was done. After the operation he felt well, and the temperature returned to normal.

On the morning of the fifth hospital day the patient was in a cheerful mood, having spent a comfortable night. As the nurse was about to give him breakfast, he suddenly complained of pain in the back. He then began to breathe deeply, became flushed and died in a few seconds.

Differential Diagnosis

Dr. Edward F. Bland: The abruptness of the onset of illness in this previously well man and his sudden and unexpected demise a few days later, with pain, breathlessness and collapse, point unmistakably to a major vascular accident. The likeliest possibilities that immediately come to mind are pulmonary embolus, coronary thrombosis and dissecting aneurysm of the aorta. It is perhaps unnecessary to go beyond those three conditions in a discussion of the differential diagnosis. There are some clinical details, however, that are puzzling and warrant special comment.

Before we embark on the discussion, may we see the x-ray films? After Dr. Hale has presented the

series of films I have a few questions that I should like to ask him. I have not seen the films.

DR. CLAYTON H. HALE: Unfortunately the films were all taken with the patient in bed and are not entirely satisfactory. We have here a heart that is somewhat enlarged, especially in the region of the ventricles. The aorta is tortuous, and there is a suggestion in one of the films that the ascending aorta is slightly widened.

DR. BLAND: Three sets of films are described. I am particularly interested in the one taken on admission.

DR. HALE: In the first film there is a rather hazy area of density in the left lower lobe and a fairly tortuous aorta. The right hilum is more prominent than the left. I do not believe that we have ever made a preautopsy diagnosis of massive pulmonary embolus by x-ray examination, although a review of the films of some of these cases has suggested that the involved pulmonary artery was larger than normal. We cannot make such a diagnosis from these films, but one would have to think of it as a possibility. The shadow in the lungs is not typical of an infarct. On the lateral film taken two days later you can again see an area of density, but this also does not look like an infarct. It looks more like an area of atelectasis in the lower lobe. The costophrenic sinus is slightly obscured, possibly by a small amount of fluid.

Another diagnosis that we have trouble in making by x-ray examination is dissecting aneurysm of the aorta. Looking back over the films of some of these cases, after the diagnosis has been proved, has suggested to us that the loss of definition of the descending aorta in the lateral projection may be a significant sign in making a diagnosis of dissecting aneurysm of the aorta. On the lateral chest films of this case the descending aorta is not clearly seen, but these are not good films, so that I do not know how much we should depend on the sign in this case.

To sum up what I have said, this man had a large heart, with no evidence of pulmonary edema. I see no characteristic shadows of infarcts. I interpret the shadow in the lower lobe as consistent with atelectasis, and the ascending aorta looks widened. This undoubtedly was a sclerotic aorta. The significance of the prominent right pulmonary artery is questionable. The absence of sharp definition of the aortic shadow below this point in the descending aorta must make one think of the possibility of a dissecting aneurysm, but one cannot safely make this diagnosis because of the poor quality of the available films.

DR. BLAND: Do you want to comment on this streak in the left upper chest?

DR. HALE: I should think that it was a small area of atelectasis.

DR. BLAND: Could it represent a healed infarct?

DR. HALE: It could, but its shape and location are rather unusual for an infarct.

DR. BLAND: In looking back over the history, it is clear that this patient had phlebitis. He had swelling of one leg and pain in the other, so that it must have been a fairly extensive process. I suspect that he had had phlebitis longer than the record indicates, indeed that he had it before he came into the hospital. That is somewhat supported, I think, by the scar in the lung, which looks to me as if it could easily be one of the scars that Dr. Castleman and Dr. Hampton[1] have so well described. He had, in addition to the phlebitis, clinical evidence of pulmonary emboli. The onset of his illness qualifies well. Its abruptness is mildly against coronary thrombosis and much more in favor of a large pulmonary embolus or a dissection of the aorta. The fact that the electrocardiogram, except for the irritability of the heart, was essentially normal should not disturb us too much in the diagnosis of pulmonary embolus.

DR. BENJAMIN CASTLEMAN: Two more electrocardiograms were taken that are not recorded in the clinical abstract.

DR. BLAND: As I look at them quickly I should say that they are essentially normal. There is no prominence of the S waves in Lead 1 or of the Q waves in Lead 3, which sometimes occurs during the first few hours after a large embolus. There is no inversion of the T waves in Lead 3, and no tendency to right-axis deviation. It should be remembered, however, that only about 10 per cent of patients with pulmonary embolus get acute cor pulmonale and that we believe the electrocardiogram is simply a reflection of the acute dilatation of the right side of the heart. It is evidence of considerable weight against coronary thrombosis, and it helps us only in a negative fashion in our consideration of possible dissection of the aorta.

When we examine the recorded findings in the heart for evidence of acute cor pulmonale, in addition to the electrocardiogram, the usual things that we look for are not commented on — namely, accentuation of the pulmonic second sound, and gallop rhythm — and certain murmurs that we should not expect to find in this condition are mentioned. Tachycardia and irritability of the heart are quite frequent with pulmonary emboli. Usually it is ventricular irritability that predominates. Therefore, we must conclude that there is nothing in the heart on first examination to indicate acute right-sided dilatation. The patient's subsequent course, however, indicates that he must have had pulmonary emboli and infarction. The transient changes described in the x-ray films seem to fit in very well with Dr. Hampton and Dr. Castleman's description of incomplete infarction of the lung, in which the shadows clear up quickly, thus indicating functional infarction without actual destruction of the pulmonary tissue. Then, of course, the

pleuritic pain and the blood spitting strongly support this impression. This man's veins were tied. Could he have died of pulmonary embolus if both femoral veins were tied? It does not state in the text the site of ligation, whether it was above or below the femoris profunda. Dr. Linton pointed out at Grand Rounds this morning that one group in this hospital prefers the lower site, whereas the other prefers the upper site. It is still possible that a large embolus could have come from the profunda if ligation was below this vein. Dr. Linton also mentioned that even after ligation 5 per cent of patients may still have serious pulmonary emboli. I am inclined to think that this patient fits into the group in which an embolus either originated in the profunda or formed above the site of ligation. Does anyone know whether the profunda was below or above the site of ligation in this patient?

DR. CASTLEMAN: The superficial femoral veins were ligated just below the point where the profunda enters to form the common femoral.

DR. BLAND: It was possible, then, for an embolus to have come from above the site of the ligature or from the profunda.

We come next to a consideration of coronary thrombosis, and I am willing to exclude that diagnosis rather quickly. The onset was too abrupt. The patient had never had trouble previously. The electrocardiograms do not suggest coronary thrombosis, the patient was well between episodes, and he died abruptly. A few years ago Currens[2] pointed out the fact that, following pulmonary embolus, the accompanying shock and lowering of blood pressure predispose to coronary thrombosis or myocardial infarction. But as an added complication here that is unlikely.

The third condition is dissection of the aorta. The abrupt onset of pain during physical labor is always suggestive of such, especially when there is radiation of the pain through to the back bilaterally. It is not known whether or not the patient had had hypertension shortly before his illness. No mention is made of arterial pulsations in the legs, but I assume it would have been mentioned if they were absent, because the legs were the object of so much consideration.

DR. PAUL D. WHITE: The pulsations were all right.

DR. BLAND: Is there anything else that points to aortic dissection? One thing that is disturbing is the diastolic murmur. We have to account for it on some basis, especially if we rely on the statement that it was not there one year before the patient came to the hospital. What could take place in the course of a year in a person who was otherwise in good health that would give a diastolic murmur of this nature? The description is not quite adequate to go into a discussion of whether it was a mitral or an aortic diastolic murmur or possibly came from some other valve. Since it was so well heard over the base and since mitral diastolic murmurs, even loud ones, are not widely transmitted, I am inclined to think that this murmur came from the aortic valve. It is unlikely that rheumatic infection in a well man at this age could produce this much heart disease in the course of a year, at least a murmur of this degree and nature. It is unlikely that syphilis was responsible: the presence of a negative Kahn test one year before admission is strong evidence against it. What can arise acutely in the heart with a resulting diastolic murmur at the base? In patients with dissecting aneurysm of the aorta the dissection occasionally proceeds in a retrograde fashion, thereby distorting the orifice and resulting in a diastolic murmur. A ruptured aortic valve usually occurs acutely and often gives rise to a high degree of aortic regurgitation. We have no evidence of such here.

DR. WHITE: The chief murmur was diastolic in time, about Grade II and best heard along the left sternal border. It sounded like the murmur of aortic regurgitation. The systolic murmur was extremely slight.

DR. BLAND: Do you think that the diastolic murmur might have been overlooked a year before entry?

DR. WHITE: It was not heard at an outside hospital. We wondered if the examination had been careful enough to exclude it at that time. We did not believe that we could place much reliance on the recent development of the murmur, but nevertheless it was one of the findings seriously considered.

DR. BLAND: It is disturbing in relation to my favored diagnosis of pulmonary embolism. The weight of clinical evidence, however, favors phlebothrombosis, with multiple pulmonary emboli and a terminal massive embolus.

DR. WHITE: This patient was obviously a difficult diagnostic problem. In fact the resident, the interns and I all differed in our diagnoses. It would, however, have been helpful for Dr. Bland actually to have seen the patient and to have talked with him as we did. All this does not get into the record. The suddenness of the onset was striking. He was working on a cruiser in the Navy Yard in a cold rain and was unusually active that day; at the height of his activity, or just as he stopped, he had a sudden overwhelming pain. It was really severe pain. He described it in different ways on different days, but he told me that he felt as if an atomic bomb had hit him, which was very descriptive and colored my opinion about as much as did anything else. Moreover, the pain radiated to the scapulas. The presence of the aortic diastolic murmur, I thought, was important as well. There seemed to be evidence of pulmonary embolism, because of the x-ray films and the blood-spitting, and yet we were never convinced that that was the diagnosis. We thought that it might have been a red herring or a complication. The picture did

not resemble coronary thrombosis in its onset; it was too abrupt. We were also quite sure that with such a severe coronary occlusion there would have been a significant change in the electrocardiogram. I was disappointed, after the x-ray diagnosis, that the electrocardiogram did not show evidence of an acute cor pulmonale. If he had had a massive enough pulmonary embolism to produce this picture he ought to have had electrocardiographic evidence of an acute cor pulmonale, which he did not have. Yet as we went on, we wondered if he might not have been an exception to the rule.

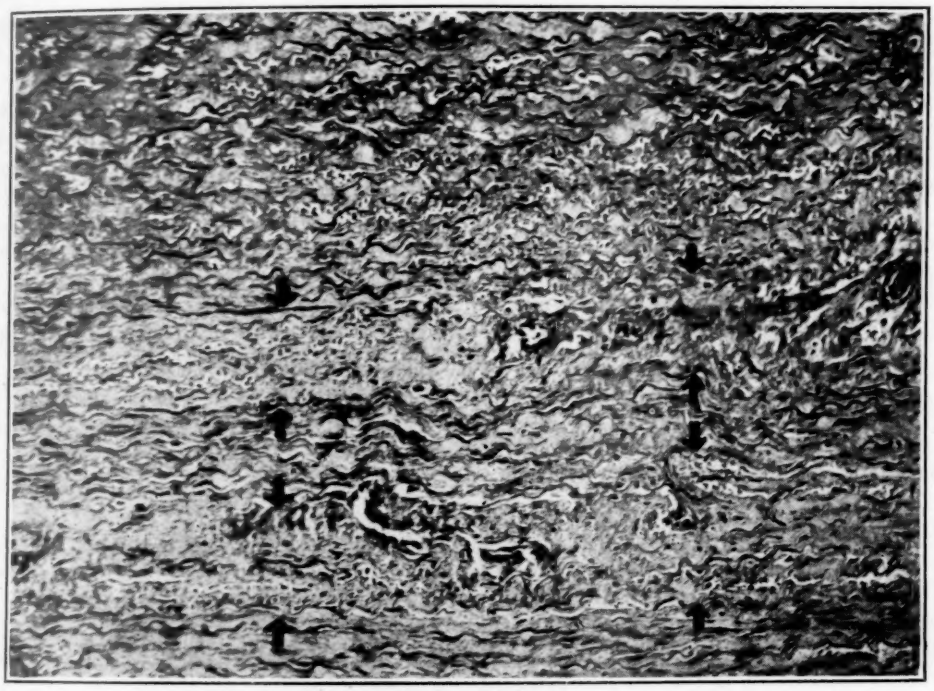

FIGURE 1. *Photomicrograph Showing Medial Degeneration in the Wall of the Aorta. In the areas outlined by the arrows, there is focal loss of the coarse black elastic fibers; this occurs before actual cyst formation takes place.*

DR. BLAND: Which possibility did you favor, DR. WHITE?

DR. WHITE: A dissecting aneurysm of the aorta because of the abrupt onset, the terrific pain and the essentially negative electrocardiogram.

CLINICAL DIAGNOSIS

Dissecting aneurysm of aorta?
Pulmonary embolism?

DR. BLAND'S DIAGNOSES

Phlebothrombosis, femoral.
Pulmonary embolism and infarction.

ANATOMICAL DIAGNOSIS

Dissecting aneurysm of aorta, with rupture into pericardium.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed a dissecting aortic aneurysm. The intimal tear was in the ascending aorta — the usual place. The dissection had extended proximally and distally — proximally to the base of the aortic valve around the coronary mouths, with some dissection of the coronaries themselves, and distally to 4 cm. above the bifurcation of the aorta. It did not reach the iliac arteries, as is so often the case. There was some dissection into the branches at the arch. The aneurysm had ruptured through the adventitia at the level of the intimal tear into the pericardium, with resultant cardiac tamponade.

DR. WHITE: Were the renal arteries involved?

DR. CASTLEMAN: No.

The lungs were quite disappointing. We were unable to find emboli or infarcts.

DR. BLAND: But he was spitting blood and had pleuritic pain.

DR. CASTLEMAN: There were areas of atelectasis and congestion, but nothing that we could call a true infarct. It is quite possible, as you suggested, that they were incomplete infarcts that had begun to disappear. At any rate there was no massive embolus, and no large infarct.

DR. BLAND: Is that shadow part of the dissection of the aorta?

DR. CASTLEMAN: The ascending aorta was diffusely dilated, which may have been the result of hypertension or perhaps a combination of hyper-

tension and medial degeneration, which was quite severe.

DR. WHITE: I think that he had a hypertensive aorta. The x-ray films did not establish the diagnosis of dissection, but often the root of the aorta is as prominent in hypertension as in syphilis. I think that most of the right-sided vascular shadow is aorta rather than pulmonary artery.

DR. CASTLEMAN: We did not find much blood in the dissected part of the aorta.

DR. WHITE: Once in a while that is the case.

DR. CASTLEMAN: I believe that we have had only two cases with actual thrombosis in the dissecting channel. Usually the aneurysm is empty or has a few shreds of post-mortem clot. It is only when there is a large thrombus in the aneurysm that it might be possible to see an enlarged shadow by x-ray.

DR. WHITE: This could be simply the x-ray picture of a hypertensive aorta. A negative finding does not rule out a dissecting aneurysm, whereas a positive finding may be helpful.

DR. CASTLEMAN: This medial degeneration of the wall of the aorta was first described by Erdheim[3,4] and called by him "medionecrosis aortae idiopathica cystica," because occasionally the chromatropic degenerative material breaks down to form small cysts (Fig. 1). This condition was described in this country for the first time by Dr. Alan Moritz.[5] He is here today and perhaps will comment on it.

DR. ALAN R. MORITZ: I believe that there is still skepticism in some quarters regarding the occurrence of cystic medial necrosis of the aorta independent of atherosclerosis. I am sure that such skepticism is unjustified. It is true, however, that minor and, from a functional standpoint, inconsequential cystic medial changes are frequently seen both with and without intimal disease and that such changes should be extensive if they are to be held responsible for aortic rupture. In my experience aortic rupture due to cystic medial necrosis is likely to run a more rapidly fatal course than that due to atherosclerosis.

DR. WHITE: In our series,[6] the reverse is true. Several days usually elapse before death.

DR. MORITZ: I have only seen ten or twelve cases of aortic rupture due to cystic medial necrosis, but I am sure that the majority of these patients died within minutes or, at the most, a few hours after the aorta gave way.

DR. CASTLEMAN: Our experience here is that in cases that have a dissecting aortic aneurysm the intimal tear has always been on the basis of medial necrosis, rather than being due to atheromatous ulceration. In fact, the intima is usually quite smooth in the region of the tear. In those cases in which dissection did originate from an arteriosclerotic ulceration, the dissection was very short and was an incidental autopsy finding, not having caused any clinical symptoms.

DR. WHITE: This man lived for four and a half days. Is that the average?

DR. CASTLEMAN: Yes.

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"DIPHTHERIA REBOUNDS"

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cribed largely to greater awareness of the disease, which resulted in early diagnosis, better isolation and prompt treatment with antitoxin. After the rise of the Nazis, however, diphtheria began to increase in incidence and in severity, largely owing to the fact that immunization had not been practiced on any large scale.

During the period immediately preceding the outbreak of war, the countries neighboring on Germany were still having low diphtheria rates. So long as communications and the exchange of populations between Germany and her neighbors were still limited, the trends of diphtheria incidence remained the same in each of these countries. After the beginning of the war, however, Germany began to "export" diphtheria with her troops. The neighboring victims of German aggression were thus faced with a disease that had had a relatively low incidence for some time, during which a new generation of susceptibles had grown up because of the lack of effective programs of immunization. As a result, there was a tremendous increase in diphtheria in many of these countries at a time when it was almost impossible to apply effective countermeasures. The only country that did not share in this great increase of incidence was Hungary, in which an extensive immunization program had been practiced just prior to its occupation by Germany. This program paid dividends by holding the diphtheria rates to reasonably low levels, and the increase that did occur could be accounted for by changes in the population.

The number of cases of and deaths from diphtheria in the United States has shown a decline, with few remissions, since the beginning of this century, and there has been a steady and sharp drop since 1920. Immunization against this disease has been practiced only on a voluntary basis and in general has been quite spotty throughout the country. Without doubt, many American troops in Europe have become carriers of virulent diphtheria bacilli, irrespective of whether they have had the disease. Those who are yet to return will have had a greater exposure and will undoubtedly carry with them a greater volume of potential infection. To prevent any serious outbreak in this country it is therefore urgent that efforts at extending immunization against diphtheria be redoubled.

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5:45–6:30. Poliomyelitis. Conrad Wesselhoeft: physician-in-chief, Haynes Memorial, Massachusetts Memorial Hospitals; clinical professor of communicable diseases, Harvard Medical School and Boston University School of Medicine.

7:30–8:15. Colds, Influenza and Pneumonia. Maxwell Finland: chief, Fourth Medical Service, and associate physician, Thorndike Memorial Laboratory, Boston City Hospital; assistant professor of medicine, Harvard Medical School.

8:15–9:00. Progress Report. Charles A. Janeway: assistant professor of pediatrics, Harvard Medical School; visiting physician, Children's Hospital; associate in medicine, Peter Bent Brigham Hospital.

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3:00–3:45. Chronic Rheumatic Heart Disease: Diagnosis and treatment. Edward F. Bland: instructor in medicine, Harvard Medical School; visiting physician, House of the Good Samaritan; assistant visiting physician, Massachusetts General Hospital.

3:45–4:30. Arterial Hypertension and Its Treatment. Robert W. Wilkins: associate professor of medicine, Boston University School of Medicine; member, Evans Memorial, Massachusetts Memorial Hospitals.

4:30–5:15. Electrocardiography in General Practice. James M. Faulkner: professor of medicine, Tufts College Medical School.

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5:45–6:30. Cardiac Arrhythmias: Their significance and treatment. Louis Wolff: instructor, Courses for Graduates, Harvard Medical School; chief, Cardiac Clinic, Beth Israel Hospital.

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3:00–3:45. Congenital Heart Disease: Indications for surgical treatment. C. Sidney Burwell: physician, Peter Bent Brigham Hospital; consultant, Children's Hospital.

3:45–4:30. Peripheral Vascular Disease and Its Treatment. E. Everett O'Neil: clinical professor of surgery, Boston University School of Medicine; visiting surgeon, Boston City Hospital.

4:30–5:15. Discussion of Cardiovascular Problems and Replies to Questions from Physicians. Herrman L. Blumgart: physician-in-chief, Beth Israel Hospital; faculty instructor, Harvard Medical School.

5:15–6:00. Discussion of Cardiovascular Problems and Replies to Questions from Physicians. Burton E. Hamilton: cardiologist, Boston Lying-in Hospital; lecturer in Cardiology, Boston City Hospital.

March 4. Pharmacology and Therapeutics. *Chairmen*: Donald G. Anderson and Chester S. Keefer.

5:00–5:45. Sedatives and Analgesics. Robert W. Wilkins: assistant professor of medicine, Boston University School of Medicine; member, Evans Memorial, Massachusetts Memorial Hospitals.

5:45–6:30. Streptomycin. Chester S. Keefer: Wade Professor of Medicine, Boston University School of Medicine; director, Evans Memorial, Massachusetts Memorial Hospitals.

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8:15–8:45. Sulfonamides. Francis C. Lowell: associate professor of medicine, Boston University School of Medicine; member, Evans Memorial, Massachusetts Memorial Hospitals.

March 6. Nutritional Diseases and Vitamin Therapy. *Chairmen:* Harold J. Jeghers and Fred J. Stare.

3:00–3:35. Nutritional Diseases in General Practice. Harold J. Jeghers: assistant professor of medicine, Boston University School of Medicine; physician and chief of Fifth Medical Service, Boston City Hospital.

3:35–4:10. A Review of Recent Advances in Nutrition. Fred J. Stare: associate professor of nutrition, Harvard University; associate in medicine, Peter Bent Brigham Hospital.

4:10–4:45. Nutritional Therapy. Charles Davidson: assistant in medicine, Harvard Medical School; resident physician, Thorndike Memorial Laboratory, and resident director, Second and Fourth Medical Services, Boston City Hospital.

Public Health. *Chairman*: Vlado A. Getting.

4:45–5:25. Recent Developments in Public Health. Vlado A. Getting: Commissioner of Public Health, Commonwealth of Massachusetts.

Industrial Medicine. *Chairman*: Daniel L. Lynch.

5:25–6:00. The Objectives of Industrial Medicine. George F. Wilkins: assistant medical director, New England Telephone and Telegraph Company; associate in surgery, Peter Bent Brigham Hospital.

March 11. Blood Diseases. *Chairmen*: William B. Castle and Joseph F. Ross.

5:00–5:50. The Use of Blood and Blood Derivatives. Charles A. Janeway: assistant professor of pediatrics and instructor in bacteriology and immunology, Harvard Medical School; visiting physician, Children's Hospital; associate in medicine, Peter Bent Brigham Hospital.

5:50–6:30. The Massachusetts Civilian Blood Program. Geoffrey Edsall: instructor in applied immunology, Harvard School of Public Health; assistant director, division of Biologic Laboratories, Massachusetts Department of Public Health.

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3:40–4:00. Progress in the X-Ray Therapy of Malignant Lesions. Frederick W. O'Brien: radiologist, Boston City Hospital.

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EXECUTIVE COMMITTEE OF THE COUNCIL

On January 9, 1946, the Executive Committee of the Council, on the recommendation of the Committee on Membership and representatives from the supervising censors, took the following actions:

Allowed the following named fellows, applying for retirement and with all dues paid and in good standing, to retire under the provisions of Chapter I, Section 5, of the by-laws:

Hunter, Norman M. (Middlesex South), 98 Packard Street, Hudson.
Overlander, J. Eliot (Hampden), 167 Maple Street, Springfield.
Quest, James F. (Suffolk), 409 Marlboro Street, Boston.
Vietor, Agnes C. (Worcester), P. O. Box 188, Worcester.
Williamson, Cordelia I. (Suffolk), 464 Huntington Avenue, Boston.

Allowed the following named fellows, applying for resignation and with all dues paid and in good standing, to resign under the provisions of Chapter I, Section 7, of the by-laws:

Beaulieu, Florence A. (Hampden), Monson State Hospital, Palmer.
Margulois, Benjamin (Hampden), Monson State Hospital, Palmer.

Allowed the following named fellow to change his membership from one district society to another, without change of legal residence, under the provisions of Chapter III, Section 3, of the by-laws:

Moore, Francis D., 371 Walnut Street, Brookline (office: Boston). (Norfolk to Suffolk.)

Reinstated the following named physicians, under the provisions of Chapter I, Section 10, of the by-laws, who had been deprived of fellowship for the nonpayment of dues, provided their arrears in dues at the time of deprivation both to the Massachusetts Medical Society and to their district societies, plus their dues for the year 1946 both to the Massachusetts Medical Society and to their district societies be sent to the treasurer of the Society:

Hagerty, Harry J. (Worcester), 14 Ekman Street, Worcester.
Sullivan, Leo. J. (Bristol South), 379 Whipple Street, Fall River.

Remitted the dues owed the Society for the year 1946 of the following named fellow, who is ill and completely incapacitated and has been completely incapacitated for the past seven or eight years, under the provisions of Chapter I, Section 6, of the by-laws:

Kaufman, M. F. (Worcester), 79 Elm Street, Worcester.

The personnel of the Committee on Membership is as follows: Harlan F. Newton, *chairman*; Roy V. Baketel; William A. R. Chapin; Peirce H. Leavitt; and Samuel N. Vose. The representatives of the supervising censors were as follows: William H. Allen; H. Quimby Gallupe; and Albert E. Parkhurst.

MICHAEL A. TIGHE, M.D., *Secretary*
Executive Committee

DEATHS

KEITH — Theodore K. Keith, M.D., of Newton Center, died January 15. He was in his forty-fourth year.

Dr. Keith received his degree from Boston University School of Medicine in 1926. In 1943 he entered the Army Medical Corps, serving overseas for two years in England, France and Germany.

His widow, two sons, his mother and father and a brother and sister survive.

LEE — Frank R. Lee, M.D., of North Andover, died October 15. He was in his forty-third year.

Dr. Lee received his degree from Tufts College Medical School in 1927. He was a fellow of the American Medical Association.

ROBBINS — Fred G. Robbins, M.D., of Salem, died May 16. He was in his seventy-sixth year.

Dr. Robbins received his degree from Harvard Medical School in 1892.

His widow survives.

MISCELLANY

MACY FOUNDATION DISCONTINUES REPRINT SERVICE

Doctor Willard C. Rappleye, president of the Josiah Macy, Jr., Foundation, announces that more than five million copies of over four hundred leading medical and scientific articles have been published by the Foundation's War Reprint Service during the last three years for medical officers of the armed forces of the United States and, in so far as possible, of Canada, England, New Zealand, Australia, the Union of Socialist Soviet Republics and China. Dr. Rappleye stated that, with the plans for demobilization of the armed forces, the service was discontinued on January 1.

The War Reprint Service has been an effort to bring new and important developments in the science and practice of medicine to medical officers who were largely cut off from sources of medical information during the war. In the selection of these articles the Foundation has had the active cooperation of the Committee on Pathology of the Division of Medical Sciences, National Research Council, and of the National Committee for Mental Hygiene. The articles selected for reprint and distribution were those dealing with the most recent scientific developments that had a direct bearing on medical and health problems related to military service. The distribution to the medical officers was worked out in co-operation with the surgeons general of the Army and Navy and the Air Surgeon. Through the courtesy of the National Committee for Mental Hygiene, more than one million reprints were delivered to medical officers specializing in neuropsychiatry.

In addition to the articles reproduced from journals the Foundation published for the Air Surgeon five original monographs, prepared by medical officers of the Army Air Forces, dealing with personality disturbances occurring in combat zones. Over ninety-five thousand copies of these monographs were distributed by the War Reprint Service as official documents of the Office of the Air Surgeon. Eight additional monographs and nine reviews of medical literature on subjects of military interest were also prepared, and seventy thousand copies were distributed. Since August, 1944, a *News Letter* for the Rheumatic Fever and Streptococcus Control Program of the Army Air Forces has been published monthly for the Air Surgeon, and over one thousand copies each month have been mailed to interested medical officers, military hospitals and medical-school libraries. With the help of the Interdepartmental Committee on Cultural and Scientific Co-operation of the Department of State, sixty

thousand reprints were distributed to medical teachers and investigators in forty-eight foreign countries. The Office of War Information requested permission to circulate the Foundation's reprints among more than thirty of their foreign outposts and reduplicated selected articles for their distribution to medical leaders abroad.

NOTICES

ANNOUNCEMENTS

Dr. R. Earle Glendy, having returned from service with the United States Army, announces the opening of his office at 820 South Jefferson Street, Roanoke, Virginia, for the practice of internal medicine, with special interest in diseases of the heart and circulation.

Dr. Langdon Parsons, having returned from military service, is resuming the practice of surgery at 264 Beacon Street, Boston.

BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club in Sprague Hall at the Boston Medical Library, 8 Fenway, on Monday, February 11, at 8:15 p.m. Dr. Charles F. Branch will speak on the subject "Some Aspects of the History of Cancer."

All interested persons are cordially invited to attend this meeting.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore, Boston, on Wednesday, February 20, at 8 p.m. Dr. David C. Ditmore will speak on the subject "The Diagnosis and Treatment of Hemorrhoids, with Special Reference to Physical Medicine."

NEW ENGLAND HEART ASSOCIATION

The annual Henry Jackson Lecture under the auspices of the New England Heart Association will be given by Dr. Tracy B. Mallory at 8:15 p.m. on Tuesday, February 26, at the Boston Medical Library. His subject will be "Certain Features of the Pathology of Traumatic Shock."

Interested physicians and medical students are cordially invited to attend.

NEW ENGLAND PEDIATRIC SOCIETY

The annual meeting of the New England Pediatric Society will be held in Boston on Thursday, February 28.

HERMANN M. BIGGS MEMORIAL LECTURE

The Hermann M. Biggs Memorial Lecture under the auspices of the Committee on Public Health Relations, New York Academy of Medicine, will be delivered by Dr. Laurence H. Snyder, professor of medical genetics, Ohio State University, at 8:30 p.m. on Thursday, April 4, in Hosack Hall, New York Academy of Medicine. His subject will be "Medical Genetics and Public Health."

All persons interested are invited to attend.

ELLA SACHS PLOTZ FOUNDATION FOR THE ADVANCEMENT OF SCIENTIFIC INVESTIGATION

During the twenty-second year of the Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation, thirty-eight applications for grants were received by the Trustees, twenty-five of which came from the United States, the other thirteen coming from five different countries in Europe, Asia, North and South America. Twenty-two grants were distributed.

Applications for grants to be held during the year 1946-1947 must be in the hands of the Executive Committee before April 15, 1946. There are no formal application blanks but letters asking for aid must state definitely the qualifications of the investigator, an accurate description of the research, the size of the grant requested and the specific use of the money to be expended. In their requests for aid applicants should state whether or not they have approached other foundations for financial assistance and what other sources of support are relied on for research. It is highly desirable to include letters of recommendation from the directors of the departments in which the work is to be done. Only applications complying with the above conditions will be considered. Applications should be sent to Dr. Joseph C. Aub, Massachusetts General Hospital, Fruit Street, Boston 14.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 14

FRIDAY, FEBRUARY 15

*9:00–10:00 a.m. Diagnosis of Congenital Heart Disease by Venous Catheterization. Dr. Lewis Dexter. Joseph H. Pratt Diagnostic Hospital.

*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

10:50 a.m. Topical Therapy in Dermatology. Dr. Bernard Appel. (Postgraduate Clinic in Dermatology and Syphilology.) Amphitheater, Dowling Building, Boston City Hospital.

MONDAY, FEBRUARY 18

*12:00 m.–1:00 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

TUESDAY, FEBRUARY 19

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

WEDNESDAY, FEBRUARY 20

*9:00–10:00 a.m. Psychologic Aspects of the Menstrual Cycle. Dr. Norris T. Flanagan. Joseph H. Pratt Diagnostic Hospital.

*10:30–11:30 a.m. Medical Clinic. Isolation Building Amphitheater, Children's Hospital.

*12:00 m. Clinicopathological Conference (Children's Hospital). Amphitheater, Peter Bent Brigham Hospital.

*2:30–4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

JANUARY 7–APRIL 22, 1946. Metropolitan State Hospital. Eleventh Postgraduate Seminar in Neurology and Psychiatry. Page 314, issue of September 6.

FEBRUARY 4–MARCH 29. Health Education Institute. Page 746, issue of December 13.

FEBRUARY 9. New England Dermatological Society. Page xix, issue of January 17.

FEBRUARY 11. Boston Medical History Club. Notice above.

FEBRUARY 12. Harvard Medical Society. Peter Bent Brigham Hospital. 8:00 p.m.

FEBRUARY 13. Massachusetts Medico-Legal Society. Page xix, issue of January 17.

FEBRUARY 14. Diagnostic and Therapeutic Suggestions in Cardiovascular Disease. Dr. John Sproull. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

FEBRUARY 19. Greater Boston Medical Society. Page 168, issue of January 31.

FEBRUARY 20. Tufts Medical Alumni Lecture. Page xix, issue of January 17.

FEBRUARY 20. New England Society of Physical Medicine. Notice above.

FEBRUARY 26. New England Heart Association. Notice above.

FEBRUARY 27. Tufts Alpha Omega Alpha. Page 168, issue of January 31.

FEBRUARY 28. New England Pediatric Society. Notice above.

APRIL 4. Hermann M. Biggs Memorial Lecture. Notice above.

MAY 13–17. American College of Physicians. Page 798, issue of December 20.

DISTRICT MEDICAL SOCIETY

WORCESTER

FEBRUARY 13. Worcester State Hospital.

MARCH 13. Worcester Memorial Hospital.

APRIL 10. Hahnemann Hospital.

MAY 8. Annual meeting.